PB81-102659

# Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene, and Related Compounds

Syracuse Research Corp., NY

Prepared for

Environmental Protection Agency
Washington, DC

May 80

U.S. Department of Commerce
National Technical Information Service
NTIS

## TECHNICAL REPORT DATA

*(Please read Instructions on the reverse before completing)*

| | | |
|---|---|---|
| 1. REPORT NO.<br>EPA 560-11-80-018 | 2. | 3. RECIPIENT'S ACCESSION NO.<br>PB81-102659 |
| 4. TITLE AND SUBTITLE<br>Investigation of Selected Potential Environmental Contaminants: Styrene, Ethylbenzene, and Related Compounds | | 5. REPORT DATE<br>May 1980 |
| | | 6. PERFORMING ORGANIZATION CODE |
| 7. AUTHOR(S)<br>J. Santodonato, W.M. Meylan, L.N. Davis, P.H. Howard, D.M. Orzel, D.A. Bogyo | | 8. PERFORMING ORGANIZATION REPORT NO<br>TR 80-569 |
| 9. PERFORMING ORGANIZATION NAME AND ADDRESS<br>Center for Chemical Hazard Assessment<br>Syracuse Research Corporation<br>Merrill Lane, University Heights<br>Syracuse, New York 13210 | | 10. PROGRAM ELEMENT NO. |
| | | 11. CONTRACT/GRANT NO.<br>EPA 68-01-3250 |
| 12. SPONSORING AGENCY NAME AND ADDRESS<br>Office of Toxic Substances<br>U.S. Environmental Protection Agency<br>Washington, D.C. 20460 | | 13. TYPE OF REPORT AND PERIOD COVERED<br>Final Technical Report |
| | | 14. SPONSORING AGENCY CODE |

15. SUPPLEMENTARY NOTES

16. ABSTRACT

This report reviews the potential environmental hazard from the commercial use of four related compounds: ethylbenzene, styrene, α-methylstyrene, and divinylbenzene. Both ethylbenzene and styrene are produced in 6-7 billion pounds per year while the other two compounds are produced in much smaller quantities. Ethylbenzene is used to produce styrene and styrene and the other monomers are used to make polystyrene and other resins, elastomers, and rubbers. Significant non-commercial sources of the compounds are also possible including automobile exhaust, gasoline, and other combustion sources. Ethylbenzene and styrene have both been detected in air and water samples. Information on physical and chemical properties, production methods and quantities, commercial uses and factors affecting environmental contamination and information related to health and biological are reviewed.

17. KEY WORDS AND DOCUMENT ANALYSIS

| a. DESCRIPTORS | b. IDENTIFIERS/OPEN ENDED TERMS | c. COSATI Field/Group |
|---|---|---|
| styrene<br>ethylbenzene<br>α-methylstyrene<br>divinylbenzene<br>toxicity<br>chemistry | vinylbenzenes<br>styrenes | |

| | | |
|---|---|---|
| 18. DISTRIBUTION STATEMENT<br>Document is available to the public through the National Technical Information Service, Springfield, Va. 22151 | 19. SECURITY CLASS *(This Report)* | 21. NO. OF PAGES |
| | 20. SECURITY CLASS *(This page)* | 22. PRICE |

EPA Form 2220-1 (9-73)

PB81-102659

EPA 560/11-80-018

# INVESTIGATION OF SELECTED POTENTIAL ENVIRONMENTAL CONTAMINANTS: STYRENE, ETHYLBENZENE, AND RELATED COMPOUNDS

May 1980

Office of Toxic Substances
U.S. Environmental Protection Agency
Washington, D.C. 20460

SYRACUSE RESEARCH CORPORATION

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA 22161

EPA 560/11-80-018 TR-80-569

# INVESTIGATION OF SELECTED POTENTIAL ENVIRONMENTAL CONTAMINANTS:

## STYRENE, ETHYLBENZENE, AND RELATED COMPOUNDS

Joseph Santodonato
William M. Meylan
Leslie N. Davis
Philip H. Howard
Denise M. Orzel
Dennis A. Bogyo

May 1980
FINAL REPORT

Contract No. 68-01-3250
SRC No. 1279-07

Project Officer - Frank Letkiewicz

Prepared for:

Office of Toxic Substances
U.S. Environmental Protection Agency
Washington, D.C.

---

Document is available to the public through the National Technical Information Service, Springfield, Virginia 22151

i.a

# NOTICE

This report has been reviewed by the Office of Toxic Substances, EPA, and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Environmental Protection Agency, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

# Table of Contents

Page

EXECUTIVE SUMMARY xiii

I. Physical and Chemical Data 1

- A. Structure and Properties 1
  - 1. Chemical Structure and Nomenclature 1
  - 2. Mixtures 1
  - 3. Physical Properties of the Pure Material 3
  - 4. Properties of the Commercial Materials 6
  - 5. Principal Contaminants of the Commercial Products 11
- B. Chemical Reaction in the Environment 13
  - 1. Photochemistry 14
  - 2. Hydrolysis 15
  - 3. Liquid-Phase Oxidation 16
  - 4. Photochemical Smog Reaction 18
  - 5. Miscellaneous Reactions 22

II. Environmental Exposure Factors 27

- A. Production Aspects 27
  - 1. Quantity Produced, Imported and Exported 27
  - 2. Producers, Production Sites, and Major Distributors 30
  - 3. Current Production Methods 36
    - a. Ethylbenzene 36
      - (1) Liquid-Phase Benzene Alkylation 36
      - (2) Alkar Vapor-Phase Benzene Alkylation 40
      - (3) Fractionation of Ethylbenzene from Mixed Xylene Streams 43
      - (4) Extraction from Styrene Tars 45
    - b. Styrene 45
      - (1) Dehydrogenation of Ethylbenzene 46
      - (2) Co-Product with Propylene Oxide 49
    - c. α-Methylstyrene 49
      - (1) By-Product from Cumene-Phenol Process 49
      - (2) Dehydrogenation of Cumene 50
    - d. Divinylbenzene 50

Table of Contents (Cont'd)

Page

4. Market Price and Trends 53

  a. Ethylbenzene 53
  b. Styrene 56
  c. α-Methylstyrene 56
  d. Divinylbenzene 57

5. Quantity Produced as Contaminant of Other Materials 57

  a. Ethylbenzene and Styrene 57
  b. α-Methylstyrene and Divinylbenzene 59

B. Use Aspects 59

1. Consumption and Use Data 59

  a. Ethylbenzene 59
  b. Styrene 60

    (1) Polystyrene 60
    (2) ABS Resins 65
    (3) SAN Resins 65
    (4) Styrene-Butadiene Copolymer Latexes 66
    (5) Other Copolymers Over 50% Styrene 66
    (6) SBR Elastomers 67
    (7) Unsaturated Polyester Resins 67
    (8) Miscellaneous Polymers Less Than 50% Styrene 68
    (9) Other 68

  c. α-Methylstyrene 69
  d. Divinylbenzene 69

2. Use Sites 70
3. Application of Products Containing Contaminants 70

  a. Ethylbenzene 70
  b. Styrene 79

4. Projected or Proposed Uses 79
5. Alternatives to Use 79

C. Entry Into the Environment 80

1. Points of Entry 80

  a. Production 80
  b. Use 81
  c. By-Product or Contaminant 81
  d. Miscellaneous Disposal 82
  e. Monomer Migration from Polystyrene 82

Table of Contents (Cont'd)

Page

2. Emission and Effluent Control Methods 83
3. Production in the Environment 84
    a. Motor Vehicle Exhausts 84
    b. Combustion Systems 84
    c. Pyrolysis 86
    d. Cigarette Smoke 86
    e. Incineration 86

D. Analytical Methods 87
1. Sampling Techniques 87
2. Chromatographic Methods 93
3. Spectroscopic Methods 99
4. Electrochemical and Miscellaneous Methods 101

E. Monitoring 103
1. The Atmosphere 103
2. Water 108
3. Food and Other Ingested Materials 112
4. Industrial Products 114
5. Miscellaneous Monitoring 115

III. Health and Environmental Effects 116

A. Environmental Fate and Transport 116
1. Biodegradation 116
2. Chemical Degradation 118
3. Environmental Transport 118

B. Biological Effects 119
1. Toxicity and Clinical Studies in Man 119
    a. Occupational Studies 119
        (1) Biological Monitoring 119
        (2) Effects on Worker Health 126
    b. Epidemiologic Studies 135
    c. Controlled Metabolic Studies in Humans 137
        (1) Absorption and Excretion 137
        (2) Physiologic Effects 143
    d. Poisoning Incidents 144

## Table of Contents (Cont'd)

Page

2. Effects on Non-Human Mammals 145

    a. Absorption/Excretion Studies 145
    b. Metabolism and Pharmacology 151
    c. Acute Toxicity 156

        (1) Oral Administration 156
        (2) Vapor Inhalation 159
        (3) Skin Contact 163
        (4) Eye Contact 163
        (5) Other Routes 163

    d. Subchronic Toxicity 167

        (1) Oral Administration 167
        (2) Vapor Inhalation 169
        (3) Skin Contact 178
        (4) Parenteral Administration 178

    e. Teratogenicity 178
    f. Mutagenicity 182
    g. Carcinogenicity 194

3. Effects on Other Vertebrates 198

    a. Fish 198

4. Effects on Invertebrates 198
5. Effects on Plants 198
6. Effects on Microorganisms 202
7. Biochemical Studies 209

IV. Regulations and Standards 213

A. Current Regulations 213

1. Labelling Requirements 213

    a. Styrene 213
    b. α-Methylstyrene 213
    c. Ethylbenzene 214
    d. Divinylbenzene 214

2. Food Tolerances 214

## Table of Contents (Cont'd)

Page

3. Standards for Human Exposure 215
    a. Styrene Monomer 215
    b. α-Methylstyrene 215
    c. Ethylbenzene 216
    d. Divinylbenzene 216
4. NFPA Hazard Identification Code 216

B. Current Handling Practices 217
1. Special Handling in Use 217
    a. Styrene 217
    b. α-Methylstyrene 217
    c. Ethylbenzene 218
    d. Divinylbenzene 218
2. Storage and Transport Practices 219
    a. Styrene 219
    b. α-Methylstyrene and Divinylbenzene 220
    c. Ethylbenzene 220
3. Accident Procedures 221
    a. First Aid Procedures 221
        (1) Styrene 221
    b. Spill and Leak Procedures 221
        (1) Styrene 221
        (2) α-Methylstyrene 222
        (3) Ethylbenzene 222
        (4) Divinylbenzene 222

TECHNICAL SUMMARY 223

References 235

# List of Tables

| Number | | Page |
|---|---|---|
| 1 | Structure and Nomenclature of Styrene and Related Compounds | 2 |
| 2 | Physical Properties of Chemically Pure Styrene Compounds | 4 |
| 3 | Sales Specifications, Ethylbenzene | 7 |
| 4 | Sales Specifications, Styrene | 8 |
| 5 | Sales Specifications, α-Methylstyrene | 9 |
| 6 | Typical Commercial Product Values, Divinylbenzene | 10 |
| 7 | Typical Chemical Analysis of Styrene Monomers | 12 |
| 8 | Carbon Balance for Toluene - NOx System | 21 |
| 9 | Miscellaneous Reactions of Styrene Monomers and Ethylbenzene | 24 |
| 10 | U.S. Production of Ethylbenzene, Styrene, α-Methylstyrene, and Divinylbenzene | 28 |
| 11 | Imports and Exports of Ethylbenzene, Styrene, and α-Methylstyrene | 29 |
| 12 | Producers of Ethylbenzene, Styrene, α-Methylstyrene, and Divinylbenzene | 31 |
| 13 | Major Distributors of Styrene, Ethylbenzene, α-Methylstyrene, and Divinylbenzene | 34 |
| 14 | Market Prices of Ethylbenzene, Styrene, α-Methylstyrene, and Divinylbenzene | 54 |
| 15 | Styrene Consumption by End-Use in 1975 and Estimates for 1980 | 61 |
| 16 | Estimated Consumption of Styrene by Consumer and Industrial Product End-Use Markets - 1974 | 62 |
| 17 | Analysis of Various Grades of Polystyrene | 64 |
| 18 | Use Sites for Styrene and Divinylbenzene Monomer | 71 |
| 19 | Tradenames for Various Polymer Products | 73 |

List of Tables (Cont'd)

| Number | | Page |
|---|---|---|
| 20 | Representative Volume Compositions of Hydrocarbon Component of Vehicular Emissions | 85 |
| 21 | Sampling Methods for Styrene Monomers and Ethylbenzene | 94 |
| 22 | Chromatographic Analytical Methods for Styrene Monomers and Ethylbenzene | 100 |
| 23 | Styrene and Ethylbeznene Concentrations (ppm V/V) in California Air Samples | 105 |
| 24 | Atmospheric Monitoring Data for Styrene and Ethylbenzene | 107 |
| 25 | Styrene Identified in Water | 109 |
| 26 | Ethylbenzene Identified in Water | 110 |
| 27 | Styrene and Ethylbenzene Monitored in Water | 113 |
| 28 | Pure Culture Metabolism of Ethylbenzene and α-Methylstyrene | 117 |
| 29 | Metabolite Levels in Urine of Workers Exposed to Styrene | 121 |
| 30 | Subjective Symptoms Among Workers Processing Reinforced Polyesters | 129 |
| 31 | Retention, Biotransformation, and Elimination of Ethylbenzene and Styrene and Their Metabolites in Man | 139 |
| 32 | Skin Absorption of Styrene and Ethylbenzene | 142 |
| 33 | Percent of Administered $^{14}$C Activity Recovered in 72 Hours Following a Single Oral Dose of 50 or 500 mg/kg $^{14}$C-Styrene | 146 |
| 34 | Styrene Content in Rat Organs Following Inhalation and Dermal Exposures | 150 |
| 35 | Experimental Acute Oral Toxicity of Styrene and Derivatives | 158 |
| 36 | Experimental Acute Inhalation Toxicity of Styrene and Derivatives | 160 |
| 37 | Irritation and Injury to the Eyes of Rabbits Caused by Contact with Undiluted Materials | 164 |

## List of Tables (Cont'd)

| Number | | Page |
|---|---|---|
| 38 | Intraperitoneal $LD_{50}$ Values for Styrene and Styrene Oxide in Rats | 165 |
| 39 | Summary of Repeated Oral Feeding of Styrene and Ethylbenzene to Female Rats | 168 |
| 40 | Results of Repeated Vapor Inhalation Studies on Animals Exposed to Styrene | 170 |
| 41 | Results of Repeated Vapor Inhalation Studies on Animals Exposed to Ethylbenzene | 172 |
| 42 | Results of Repeated Vapor Inhalation Studies on Animals Exposed to α-Methylstyrene | 173 |
| 43 | Experimental Subchronic Inhalation Exposure to Styrene, α-Methylstyrene, and Ethylbenzene | 174 |
| 44 | Subchronic Effects of Styrene Administered by Injection to Experimental Animals | 179 |
| 45 | Mutagenicity of Styrene and Its Metabolites for *Salmonella typhimurium* | 183 |
| 46 | Mutagenicity of Styrene Oxide to *Salmonella typhimurium* | 184 |
| 47 | Mutagenicity of Styrene to *Salmonella typhimurium* | 185 |
| 48 | Lack of Reversion of *S. typhimurium* TA1535 by Styrene in the Presence of Different Amounts of Fortified Liver Homogenates from Arochlor 1254-pretreated Rats and Hamsters | 186 |
| 49 | Forward Mutations (ade Mutants) Induced in Yeast S. Pombe ($P_1$ Strain) | 189 |
| 50 | Forward Mutations ($azg^r$ Mutants) Induced in Chinese Hamster Cells ($V_{79}$ Strain) | 190 |
| 51 | Mutagenicity Test with Host-Mediated Assay (Mice): Gene Conversion (S. Cerevisiae, $D_4$ Strain) | 191 |
| 52 | Mutagenicity Test with Host-Mediated Assay (Mice): Forward Mutation (S. Pombe; ade Mutants; $P_1$ Strain) | 192 |

## List of Tables (Cont'd)

| Number | | Page |
|---|---|---|
| 53 | Effect of Modifiers of Microsomal Enzymes on 3-MC-Mediated Transformation and Cytotoxicity in 10T1/2C18 Cells | 197 |
| 54 | Median Tolerance Limits for Styrene and Ethylbenzene Obtained with the Moving Average-Angle and Graphical Interpolation Methods | 199 |
| 55 | Comparison of Acute Toxicity of Petrochemicals to Different Species of Fish | 200 |
| 56 | Significance of Difference Between Estimated 96-Hr $TL_m$ Values in Soft Water for Different Species | 201 |
| 57 | Vitality and Growth of Algae in Water with Addition of Styrene | 203 |
| 58 | Vitality and Growth of Algae in Water with Addition of Alpha-Methylstyrene | 204 |
| 59 | Growth and Changes in Pigmentation of Molds on Sabouraud-agar with Addition of Styrene | 205 |
| 60 | Growth and Changes in Pigmentation of Molds on Sabouraud-agar with Addition of α-Methylstyrene | 206 |
| 61 | Growth of Streptomycetes on Mineral Agar with Addition of Styrene | 207 |
| 62 | Growth of Streptomycetes on Mineral Agar with Addition of α-Methylstyrene | 208 |

## List of Figures

| Number | | Page |
|---|---|---|
| 1 | Ultraviolet Absorption Spectra of Styrene | 5 |
| 2 | Geographical Location of Production Sites for Ethylbenzene, Styrene, Divinylbenzene, and α-Methylstyrene | 35 |
| 3 | Ethylbenzene Manufacture Via Benzene Alkylation (Ethylene) | 37 |
| 4 | Alkar Ethylbenzene Process | 42 |
| 5 | Ethylbenzene Via Mixed Xylene Fractionation | 44 |
| 6 | Styrene Production Via Ethylbenzene Dehydrogenation | 47 |
| 7 | Finishing Distillations Used in the Manufacture of Commercial Divinylbenzene Monomer | 52 |
| 8 | Ethylbenzene Production by Year | 55 |
| 9 | Bead-Packed Absorber for Absorbing Styrene Monomer from Air | 89 |
| 10 | Design of Charcoal Filter and Filter Holder Containing Two Charcoal Filters in Series | 91 |
| 11 | Glass Apparatus Allowing Continuous Extraction of Charcoal Filters Using a Very Low Volume of Solvent | 92 |
| 12 | Possible Pathways for Metabolism of Styrene in Mammals | 152 |
| 13 | Probable Metabolic Pathways in the Biotransformation of Ethylbenzene | 157 |

# EXECUTIVE SUMMARY

Four commercially related chemicals have been considered in this review: ethylbenzene, styrene, α-methylstyrene, and divinylbenzene. Both ethylbenzene and styrene are each produced in 6-7 billion pounds annually; ethylbenzene from ethylene and benzene and styrene from ethylbenzene. Styrene is used in the production of polystyrene and other resins, elastomers, and rubbers. Although these production volumes are extremely high and may result in significant losses to the environment, there are other commercial sources of ethylbenzene and styrene which may be equally as large. There are approximately 10 billion pounds of ethylbenzene found per year in catalytic reformate which is blended into gasoline. Pyrolysis gasoline, which is formed during the cracking of petroleum to form ethylene, provides about 57-96 million pounds of ethylbenzene and 228-342 million pounds of styrene annually. Other possible sources of ethylbenzene and styrene include residues in polystyrene (about 3.2 million pounds of styrene and 1.9 million pounds of ethylbenzene annually), ethylbenzene from motor vehicle exhaust (280 millions pounds annually), tobacco smoke (both styrene and ethylbenzene), and other conbustion and pyrolysis processes. α-Methylstyrene and divinylbenzene are produced in much smaller quantities (61.4 and 3.4 million pounds per year, respectively) and are used as copolymers for styrene or other monomers. Styrene oxide, a commercial chemical that has not been treated in great detail in this review, is produced in 2 million pounds annually. This small production volume is significant because this styrene metabolite is mutagenic and possibly carcinogenic.

Both ethylbenzene and styrene have been detected in air and water samples. In water, concentration data are not available. Concentrations in urban air are around 0.2 to 5 ppb. In air, ethylbenzene appears to be about as stable as toluene, while the styrenes are very reactive. In smog chamber studies, α-methylstyrene was ranked as one of the most reactive chemicals and styrene was considered to be more reactive than most of the reactive olefins. Available aqueous biodegradability studies suggest that styrene and ethylbenzene can be metabolized by microorganisms. From the physical properties, it appears that bioconcentration in biological organisms is unlikely and evaporation from soil and water should be relatively rapid.

In occupational situations, human exposure to styrene, ethylbenzene, or α-methylstyrene is often associated with adverse health effects. Numerous studies have been conducted to characterize the toxic potential of styrene, whereas the toxicology of ethylbenzene and α-methylstyrene is less clearly understood. Nevertheless, all three chemicals appear to produce the same qualitative symptoms in humans who are acutely exposed, including irritation of the mucous membranes and narcosis at high exposure levels. Among workers chronically exposed to styrene, neurotoxicity involving both the central nervous system and the peripheral nerves has been noted. Detailed studies have not been conducted to characterize the effects of chronic exposure to ethylbenzene, divinylbenzene, or α-methylstyrene in humans.

Concern has recently developed over reports linking occupational exposure to styrene with an excess incidence of leukemia and lymphoma. This concern is compounded by the recent demonstration of chromosome abnormalities in a group of styrene workers. Thus far, however, sufficient confirmatory evidence has not been obtained to either establish a direct cause-and-effect relationship or to determine levels and duration of exposure required to produce such effects.

A study conducted with rats has also indicated that styrene may be carcinogenic. In addition, styrene has produced mutations in bacterial cells in the presence of a drug-metabolizing enzyme system. Most investigators believe that the potential carcinogenicity/mutagenicity of styrene is due to the metabolic formation of a reactive epoxide intermediate, styrene oxide, in the body. However, it is not clear whether normal detoxification mechanisms in the body are capable of removing certain minimum amounts of styrene oxide before physiologic harm may occur. It is not likely that ethylbenzene is metabolized via an epoxide intermediate, and thus its potential as a carcinogen/mutagen is doubtful, although little testing has been conducted. However, ethylbenzene can produce a degeneration of reproductive cells in the testes of both rabbits and monkeys.

In tests with several species of fish, ethylbenzene and styrene produced varying numbers of deaths with acute exposures at concentrations greater than 25 mg/ℓ. Neither compound appeared to have potential for cumulative toxicity. The effects of α-methylstyrene on most lower animals have never been studied.

It is not known whether adverse health or ecological effects may result from present environmental levels of styrene, ethylbenzene, or α-methylstyrene. Any effects on human health which may occur will almost certainly be less pronounced than those observed in occupational situations. However, since the carcinogenicity/mutagenicity of these chemicals is still unresolved, a true risk assessment cannot be presently made. From the data which are now available there is no reason to believe that the general population is being excessively exposed, or that lower animals and food-chain organisms are being adversely affected. However, numerous data gaps must be filled before a final evaluation can be presented.

# I. Physical and Chemical Data

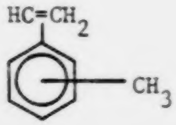
## A. Structure and Properties

### 1. Chemical Structure and Nomenclature

The four compounds which are the subject of this review are derivatives of benzene with short chain alkyl or alkenyl functional groups. Table 1 shows the molecular structure of these compounds and gives their common names, standard chemical nomenclature, and less common synonyms which have appeared from time to time in the literature.

Aside from the superficial structural similarities of their molecules, the compounds in this group of four are related to one another in their respective roles in the manufacture of polystyrene plastics: ethylbenzene as the precursor of styrene, and α-methylstyrene and divinylbenzene as copolymers with styrene. The names just used for the latter three compounds, although not standard chemical names, have become thoroughly entrenched through common usage and are retained in this review.

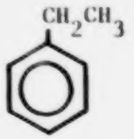
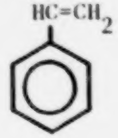
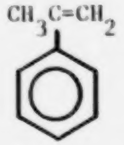
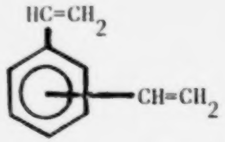
α-Methylstyrene should be distinguished from methylstyrene (methylethenylbenzene). Methylstyrene (not considered in this review) is used as a copolymer with styrene and has the following structure:



### 2. Mixtures

Divinylbenzene is manufactured by the dehydrogenation of mixed isomers of diethylbenzene. Commercial divinylbenzene therefore consists

Table 1. Structure and Nomenclature of Styrene and Related Compounds

| Compound | Common Name | Standard Chemical Name (Chemical Abstracts Nomenclature) | Synonyms |
|---|---|---|---|
|  | Ethylbenzene | Ethylbenzene | - |
|  | Styrene | Ethenylbenzene | Phenylethene<br>Cinnamene<br>Cinnamol<br>Phenylethylene<br>Styrol<br>Vinyl benzene |
|  | α-Methylstyrene | 1-Methylethenylbenzene | Isopropenylbenzene<br>2-Phenylpropene |
|  | Divinylbenzene | Diethenylbenzene | - |

principally of diluted mixtures of m- and p-divinylbenzene (Coulter and Kehde, 1970). For the commercial purposes for which this mixture is usually employed, it is not necessary to separate the isomers.

Dow Chemical Company USA (personal communication, 1977) sells divinyl benzene as a mixture of divinyl and ethylvinylbenzene isomers with a small amount of diethylbenzene also included in the mixture (see Table 6). Pure divinylbenzene (and pure isomeric mixtures of divinylbenzenes) are unstable with respect to polymerization to the extent that it is not practical to market them commercially.

### 3. Physical Properties of the Pure Material

The physical properties of the styrene compounds are summarized in Table 2. Styrene is a colorless, transparent, mobile liquid with a sweet, pleasant, characteristic odor (Boundy and Boyer, 1952). It readily undergoes aerial oxidation, producing aldehydes and ketones which impart a sharp, disagreeable odor to the styrene. Humans are capable of detecting a minimum identifiable odor of styrene at concentrations on the order of $3.4 \times 10^{-4}$ mg of 99.6% styrene per liter of air (Smith and Hochstettler, 1969).

For practical chemical purposes styrene is insoluble in water, but miscible in all proportions with a large number of commercial organic solvents such as acetone, benzene, carbon tetrachloride, methanol, ethanol, and carbon disulfide (NSC, 1971).

Styrene exhibits a strong, nearly continuous absorption of ultraviolet radiation in the range from 220 nm to 300 nm (see Figure 1). Above 300 nm the ultraviolet absorption of styrene is negligible. Consequently, styrene is not likely to be photochemically decomposed by direct adsorption of

## Table 2. Physical Properties of Chemically Pure Styrene Compounds

| | Ethylbenzene[d] | Styrene[a] | Divinylbenzene[a] | α-Methylstyrene[a] |
|---|---|---|---|---|
| Molecular Weight | 106.17 | 104.14 | 130.08 | 118.18 |
| Color | colorless | colorless | colorless | colorless |
| Boiling Point, 760 torr | 136.186°C | 145.2°C | 199.5°C | 165.38°C |
| Freezing Point, °C | -94.975 | -30.628 | -66.90 | -23.21 |
| Density (gm/ml) @20°C | 0.86702 | 0.9019 | 0.9289 | 0.9106[b] |
| Vapor Pressure, torr | 38.60 @20°C | 4.53 @20°C | 1.53 @40°C | 1.9 @20°C |
| Viscosity (cps) @20°C | | 0.730 @20°C | 1.09 | 0.940 |
| Solubility in $H_2O$, wt.% | 0.02[f] | 0.029 @20°C[e] | 0.005 @25°C[b,c] | 0.056 |

[a] Boundy and Boyer, 1952
[b] Coulter *et al.*, 1969
[c] refers to isomeric mixtures
[d] Cier, 1970
[e] NSC, 1971
[f] Union Carbide Co.

825771-U

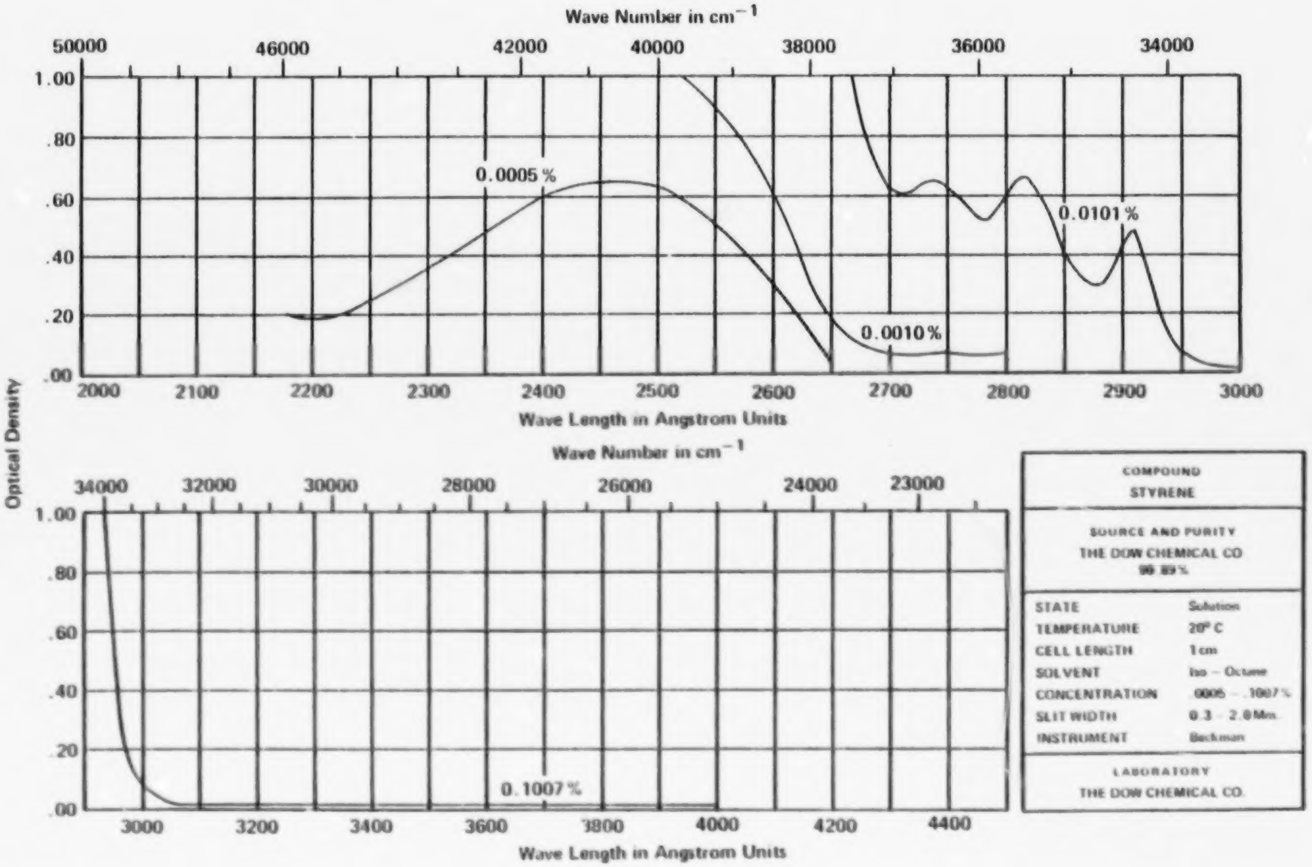


Figure 1. Ultraviolet Absorption Spectra of Styrene (Boundy and Boyer, 1952)

sunlight at the surface of the earth since sunlight contains wavelengths that are above 300 nm.

Pure monomeric α-methylstyrene is a colorless liquid (Boundy and Boyer, 1952). Its physical and chemical properties are similar to those of styrene, although it does not undergo polymerization as readily. Divinylbenzene and ethylbenzene likewise are colorless liquids, the former resembling styrene in its properties, and the latter resembling toluene and the xylenes (Cier, 1970). Divinylbenzenes are considerably less stable than styrene with respect to polymerization (Dow Chemical, 1967). Ethylbenzene has a saturated alkyl chain and does not undergo polymerization at all.

Although styrene type monomers and ethylbenzene are insoluble in water from a pratical chemical point of view, their solubility is sufficient to consider natural waterways a possible means of transport for these compounds in the environment. In general, the solubility of alkylbenzenes is a function of both the nature of the substituent chain and the positions of the substituents, if there is more than one (Sutton and Calder, 1975). On the basis of solubility studies of alkyl benzenes in distilled water and seawater (Sutton and Calder, 1975), it is likely that the styrene type monomers are all approximately 30% less soluble in seawater than distilled water. For example, ethylbenzene dissolves up to 161 ppm at 25°C in distilled water, but only 111 ppm at 25°C in seawater.

### 4. Properties of the Commercial Materials

Typical sales specifications for commercial styrene compounds are listed in Tables 3-6. These properties are very close to those of the highest purity grade available, except for divinylbenzene which is sold and

Table 3. Sales Specifications, Ethylbenzene

| | Union Carbide Corp.[a] | Monsanto Co.[b] |
|---|---|---|
| Specific Gravity @20/20°C | 0.8676 to 0.8684 | |
| Purity, % by wt., min. | 99.5 | 99.5 |
| Benzene, % by wt., max. | 0.3 | |
| Diethylbenzene, % by wt., max. | 0.2 | 0.010 |
| Free Acid | 0.005% by wt., max., as acetic acid | |
| Color (Pt-Co) | 15 | |
| Suspended Matter | Substantially free | |
| Toluene, % by wt., max. | | 0.2 |
| Xylenes, % by wt., max. | | 0.11 |
| Cumene, % by wt., max. | | 0.05 |
| Sulfur, ppm, max. | | 10 |
| Chlorides, ppm, max. | | 5 |

[a] Union Carbide Product Information Sheet, F-41645 (1969)
[b] Monsanto Product Data Sheet (1974)

Table 4. Sales Specifications, Styrene

| | Amoco Chemicals Corp.[a] | Cosden Oil and Chemical Co.[b] | Monsanto Co.[c] |
|---|---|---|---|
| Purity (wt. %), min. | 99.60 | 99.6 | 99.5 |
| Color, APHA Pt-Co, max. | 10 | 10 | 10 |
| Polymer (ppm), max. | 10 | 10 | 15 |
| Sulfur (ppm), max. as sulfur | 25 | 30 | 30 |
| Chlorides (ppm), max. as chlorine | 50 | | 100 |
| Peroxides (ppm), max. as $H_2O_2$ | 100 | 100 | 100 |
| Aldehydes (ppm), max. as benzaldehyde | 200 | 200 | 200 |
| Suspended Matter | nil | | |
| Inhibitor (ppm), *t*-butyl catechol | 12, min. | 10 - 15 | 10 - 15 |
| Specific Gravity, 20/20°C | 0.9070 - 0.9080 | | |

[a] Amoco Technical Data Sheet (1976)
[b] Cosden Oil and Chemical Co. Styrene Monomer 996 Data Sheet (1975)
[c] Monsanto Polymers and Petrochemicals Co. Data Sheet (1972)

Table 5. Sales Specifications, α-Methylstyrene

| | Clark Chemical Corp.[a] | Skelly Oil Company[b] | USS Chemicals[c] |
|---|---|---|---|
| Purity, % min. | 94.0 | 90.0 (92.3 typ.) | 98.5 |
| Phenol, % max. | 0.1 | 0.2 (typ.) | |
| Cumene, % max. | 2 | 4.3 (typ.) | |
| Butylbenzene, % max. | 2 | | |
| Acetone, % max. | 3 | 0.7 (typ.) | |
| Color (APHA), max. | 150 | | 10 |
| Residue, % typ. | | 2.5 | |
| Polymer (ppm), max. | | | 10 |
| Specific Gravity 25/25°C | | | 0.9030 - 0.9085 |
| Refractive Index (25°C) | | | 1.5340 - 1.5370 |
| Inhibitor Content, ppm | | | 10 - 20 |

[a] Clark Chemical Corporation Technical Data Sheet (1975)
[b] Skelly Oil Co., data sheet for extracted AMS (crude product stream)
[c] USS Chemicals Product Specification Sheet (1973)

Table 6. Typical Commercial Product Values, Divinylbenzene (Dow Chemical USA Material Safety Data Sheet, Divinylbenzene, 1977)

| | |
|---|---|
| Divinylbenzenes (meta and para) | 50 - 60% |
| Ethylvinylbenzene and diethylbenzene | 40 - 50% |
| Boiling Point | 383°F |
| Water Solubility | 0.0052% @25°C |
| % Volatiles by volume | 100 |
| Appearance | Pale straw liquid |
| Odor | Disagreeable |

used commercially as a mixture of the m- and p-isomers of divinyl and ethylvinyl benzenes (see Table 6). It is important that commercial grade styrene monomers be of high purity to assure predictable properties in the polymerization products which are the nearly exclusive end products of the commercial use of these compounds (except for ethylbenzene which is used almost exclusively to make styrene).

Commercial grade styrene monomers all contain a polymerization inhibitor such as t-butylcatechol (TBC). The concentration of the inhibitor varies, depending on the ease of polymerization of the monomer. Divinylbenzene may be sold with 1000 ppm TBC, α-methylstyrene with 10 ppm (Dow Chemical, 1967). Most manufacturers are willing to vary the inhibitor content of the product (usually by increasing it) according to the needs of the customer.

### 5. Principal Contaminants of the Commercial Products

As mentioned above, impurities in styrene monomers can adversely affect the properties of the polymers. Manufacturers are therefore careful to control the kind and quantity of impurities in commercial styrene chemicals and practically all commercial production of styrene chemicals come close to meeting reagent grade standards of chemical purity.

The sales specifications for ethylbenzene of the Charter Chemical Company, Houston, Texas, indicate the typical purity (99.0 to 99.2%) and impurities to be found in commercial grade ethylbenzene. The primary impurities are alkanes (paraffins) (typically, 0.5%), m- and p-xylenes (typically, 0.3%) and toluene (typically, 0.1%).

Typical chemical analyses of styrene, α-methylstyrene, and divinylbenzene are shown in Table 7. TBC is listed as an impurity in this table, but

Table 7. Typical Chemical Analysis of Styrene Monomers (Dow Chemical, 1967)

| | | Styrene | α-Methylstyrene | Vinyltoluene | Divinylbenzene |
|---|---|---|---|---|---|
| Purity | % | 99.6 | 99.3 | 99.6 | |
| Polymer | ppm | none | none | none | 5 |
| Phenyl Acetylene | ppm | < 5 | | 58 | |
| Aldehydes as CHO | ppm | 10 | 10 | 10 | 40 |
| Peroxides as $H_2O_2$ | ppm | 5 | 3 | 5 | 5 |
| Chlorides as Cl | ppm | 10 | | 5 | |
| Sulfur as S | ppm | 10 | | | 230 |
| TBC | ppm | 12 | 15 | 12 | 1000 |
| Beta-Methylstyrene | % | | 0.5 | | |
| Isopropylbenzene | % | | 0.2 | | |
| meta Vinyltoluene | % | | | 60 | |
| para Vinyltoluene | % | | | 40 | |
| Total Divinylbenzene | % | | | | 55.0 |
| meta Divinylbenzene | % | | | | 36.4 |
| para Divinylbenzene | % | | | | 18.6 |
| Total Ethylvinylbenzene | % | | | | 48.0 |
| meta Ethylvinylbenzene | % | | | | 25.0 |
| para Ethylvinylbenzene | % | | | | 13.0 |

it is, of course, added intentionally as a polymerization inhibitor. It counteracts the effects of peroxides, which are good polymerization catalysts and may account for minor variations in polymerization rates observed for different batches of styrene (Dow Chemical, 1967). Aldehydes in the styrene monomers tend to promote attack on metals such as copper. Elemental sulfur reduces the molecular weight of the polymer product and catalyzes the photochemical decomposition of the polymer (Dow Chemical, 1967). Unreacted ethylbenzene may also be present in styrene monomer, although it is not listed in Table 7. In concentrations larger than 0.5% ethylbenzene has an appreciable effect in reducing the molecular weight of polymerized styrene. Because it cannot become part of the polymer chain, any residual ethylbenzene in the polymer tends to evaporate, producing undesirable physical blemishes (Dow Chemical, 1967).

Hannah et al. (1967) used gas chromatography to determine impurities in four commercial samples of 55 to 60% divinylbenzene solution. In addition to about a dozen unidentified compounds, the following were found in one or more of the samples: benzene, toluene, ethylbenzene, cumene, ethyltoluene, styrene, α-methylstyrene, m and p-diethylbenzene, vinyltoluene, m and p-ethylvinylbenzene, napthalene, and 1,2-dihydronapthalene.

## B. Chemical Reaction in the Environment

The environmental chemistry of ethylbenzene, styrene or analogous vinyl benzenes has not been definitively studied. Their study has mostly been confined to research of importance to styrene polymerization and a few general works. The only relevant publications are limited to smog chamber studies to evaluate and rank the relative reactivity of various hydrocarbons (Levy, 1973).

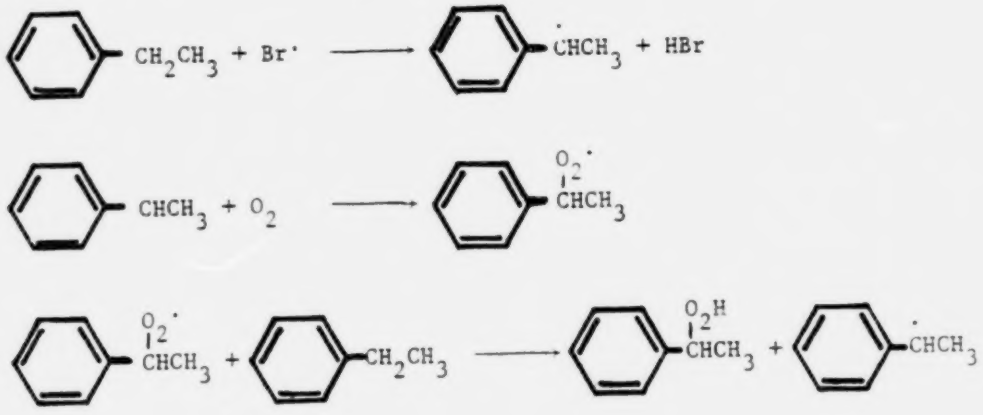
To evaluate environmental chemistry this report has drawn heavily upon mechanistic studies of analogous hydrocarbons as well as upon the known reactions of the specific hydrocarbons under study. The discussion includes information published in the classic treatise on styrene chemistry (Boundy and Boyer, 1952).

To facilitate discussion, the environmental chemistry is separated into four parts: (a) photochemistry, (b) hydrolysis, (c) liquid phase oxidation, and (d) photochemical smog reactions.

### 1. Photochemistry

Although relatively little information is available concerning the photochemistry of ethylbenzene, styrene or its analogs, the available information suggests that the compounds under study are not photoreactive in sunlight. Styrene does not absorb above 300 nm, the cut-off for sunlight reaching the earth's surface.

The irradiation of ethylbenzene in cyclohexane solution containing mercuric bromide at 254 nm gives acetophenone at approximately 17% yield (Friedman _et_ _al_., 1971). This oxidation was assigned a free radical chain mechanism. According to Friedman and coworkers the irradiation caused formation of bromide atoms which then abstract benzylic hydrogen atoms. The benzylic radicals then oxidize _via_ a radical chain mechanism which probably involved a benzyl hydroperoxide intermediate:



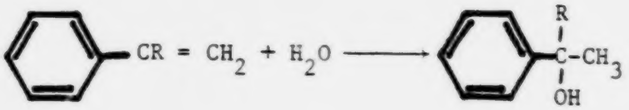
Acetophenone was also formed when ethylbenzene was irradiated without mercuric bromide, but the yield was only 5%.

γ-Radiation of ethylbenzene produces a variety of products due to the formation and recombination of many free radicals (Yamamoto et al., 1971). The products include ethane, toluene, biphenyl, and diphenylpropane. As in the above case, these reactions are probably of little significance in the environmental chemistry of ethylbenzene.

2. Hydrolysis

Although relatively little information was available concerning hydrolysis of ethylbenzene or the vinylbenzenes, some reasonable conclusions can be drawn from their known chemistry and reaction mechanisms.

The vinyl benzene should hydrolyze as expected of olefins (March, 1968). The reaction rate is expected to be acid catalyzed and negligible at pH's near neutral. The main product expected is the secondary alcohol from styrene (or the tertiary alcohol from α-methyl styrene):



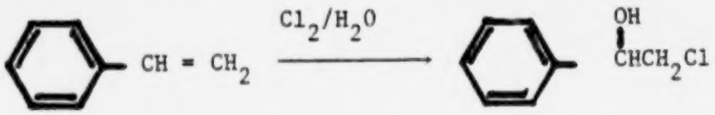
Although Boundy and Boyer (1952) mention a patent (U.S. #1,907,317) which claims hydration of styrene to yield a mixture of α- and β-phenylethanols, no experimental information was supplied.

Ethylbenzene is expected to be inert to aqueous hydrolysis. When treated with very strong acids and at high temperatures, dealkylation can proceed via a retro-Friedel-Crafts reaction (see Miscellaneous Reactions) (March, 1968).

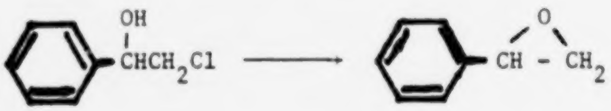
### 3. Liquid-phase Oxidation

Styrene is easily oxidized by common oxidants. This is relevant since some of these oxidants are used for water treatment.

Aqueous chlorine (hypochlorous acid) and other aqueous halogens add to styrene to yield chlorohydrin. The main product is expected to be β-chloro-α-phenylethanol (March, 1968; Boundy and Boyer, 1952):

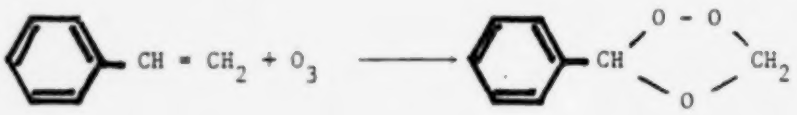


However, Boundy and Boyer (1952) have reported a British patent that claims a mixture of the above with its isomer, α-chloro-β-phenylethanol. No experimental details were present. A potential hazard would result for epoxide formation by internal $S_N2$ reaction:

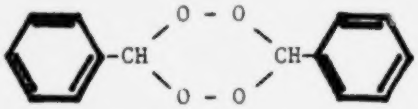


The product, styrene oxide, is a known carcinogen (IARC, 1976). Although the reaction is known to occur in alkali, no information was available to conclude if the epoxide forms in significant quantities at conditions present at water treatment.

Styrene apparently ozonates by the expected route. An intermediate product appears to be the oxonide:



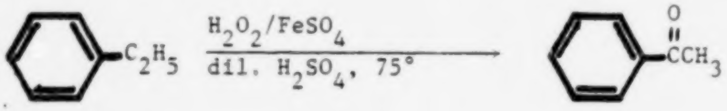
The oxonide can collapse to yield benzaldehyde and formic acid. In addition, a dimeric benzaldehyde-peroxide was identified from ozonation in carbon tetrachloride solution (Boundy and Boyer, 1952):



Ozone also initiates polymerization of pure styrene.

Styrene is oxidized by a variety of other oxidants, including hydrogen peroxide, permanganate, and nitric acid (Morrison and Boyd, 1974; Boundy and Boyer, 1952). Mild oxidizing conditions produce glycols, while strong conditions yield benzaldehyde and/or benzoic acid.

Relatively strong oxidants are required to oxidize ethylbenzene, as with all alkyl benzenes, to yield benzoic acid (Morrison and Boyd, 1974). Milder oxidants react with ethylbenzene to form acetophenone (Hotta and Suzuki, 1968):



Molecular oxygen reacts with the vinyl benzenes. If pure, liquid styrene is exposed to air, the oxygen present initiates polymerization. The oxygen reacts to form peroxides which are the polymerization chain initiators of polystyrene. Higher oxygen concentrations than normally present in air yield high molecular weight styrene peroxides. The products of slow oxidation of styrene with oxygen give positive results with tests for carbohydrates such as Fehling's and Tollen's (Boundy and Boyer, 1952). This suggests that products contain polyol groupings.

α-Methylstyrene is slowly oxidized by air to a mixture of acetophenone, aldehydes, and peroxides (Boundy and Boyer, 1952). These products increase the polymerization rate of α-methylstyrene.

Exposure of divinylbenzenes to air and direct sunlight induces their oxidation to aldehydes and peroxides. Divinylbenzene mixtures are much more susceptible to oxidation and polymerization than α-methylstyrene, and hence require greater concentrations of inhibitors (about ten times higher) to stabilize the commercial product.

### 4. Photochemical Smog Reaction

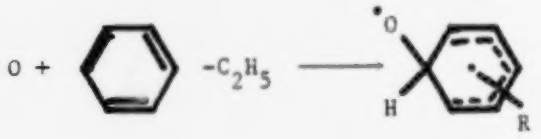
Although styrene and ethylbenzene are very reactive in photochemical smog production, the reactions and products have not been clearly delineated. The likely reactions and products from the styrenes and ethylbenzene are discussed, herein, based upon the information available from photochemical smog chamber studies.

Styrenes and ethylbenzenes are among the most active generators of photochemical smog (Levy, 1973; Laity et al., 1973, Darnall et al., 1976; Altschuller and Bufalini, 1971). The relative ranking of photochemical reactivity is an empirical method based upon parameters of the smog (Levy, 1973) or indices related to the kinetics of hydrocarbon reactions with radical species associated with photochemical smog production (Darnall et al., 1976).

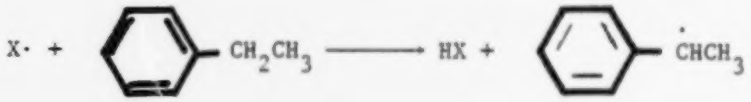
Parameters for ranking photochemical smog reactivity include rate of hydrocarbon disappearance, oxidant production, formaldehyde production, eye response, and time for maximum $NO_x$ production. In general, the most reactive class of organics are the olefins and the next most reactive class are the alkyl aromatics (Laity et al., 1973; Darnall et al., 1976; Stephens, 1973).

Olefin reactivity increases with increasing substitution of alkyl or aromatic groups at the double bond. While α-methylstyrene is ranked as one of the most reactive chemicals, styrene is ranked slightly less reactive but still among the more reactive olefins. Ethylbenzene is ranked at about the same as toluene (Levy, 1973; Laity et al., 1973; Darnall et al., 1976).

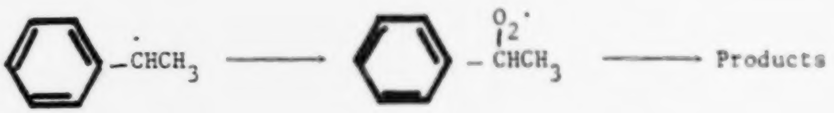
Ethylbenzene reactions under photochemical smog conditions appear consistent with the reactions proposed for toluene. Laity et al. (1973) suggest that the two most important reactions are the electrophilic addition of radical species to the aromatic ring and radical reactions at the α-carbon. Radical species, including triplet oxygen atoms and hydroxyl radicals apparently add to the ring:



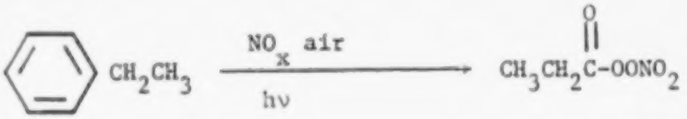
The preferred orientation would be ortho and para, addition since these would yield maximum radical stabilization. α-Hydrogen abstraction is also expected to participate in photochemical smog formation:



One of the expected reactions of benzyl radical is to add molecular oxygen and yield the peroxyl radical



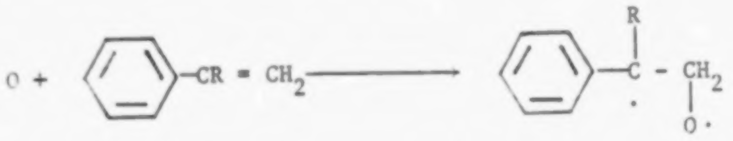
Laity et al. (1973) have identified peroxypropionyl nitrate as a product of smog chamber reactions.



Reactivities of ethylbenzene and toluene are similar. Pitts and coworkers (Darnall et al., 1976; Lloyd et al., 1976) have measured their reaction rates with hydroxyl radical. They reported second order rate constants of $4.8 \times 10^9$ and $3.6 \times 10^9$ liter/mole-sec for ethylbenzene and toluene, respectively, at 305°K.

Relatively little information was found which describes products from smog chamber oxidations of the monoalkyl aromatics. The only detailed report found was a material balance study for toluene (Spicer and Jones, 1977). They were able to identify eight products, Table 8. Similar products are expected from ethylbenzene irradiation. The expected products include peroxyacetylnitrate (PAN), peroxypropionyl nitrate, acetophenone, α-phenylethanol, and ethylphenols.

The styrenes are more reactive in photochemical smog production than the alkyl aromatics. The most important reaction in their decomposition appears to be electrophilic addition (by atomic oxygen, ozone, and other species) to the olefinic bond (Laity et al., 1973; Cvetanovic, 1963).



Pitts and coworkers (Lloyd et al., 1976; Darnall et al., 1976) measured reaction rates for a number of aliphatic olefins with hydroxyl radical, but no

Table 8. Carbon Balance for Toluene - NOx System

| | Concentration, ppm |
|---|---|
| Initial toluene | 24.1 |
| Carbon-containing compound identified after 4 hours of irradiation, total | 17.3 |
| Unreacted toluene | 12.3 |
| PAN (peroxyacetyl nitrate) | 0.6 |
| Benzaldehyde | 2.4 |
| Tolualdehyde | 0.1 |
| Phthaldehydes | 0.7 |
| Phenol | 0.1 |
| Cresols | 0.7 |
| Benzyl alcohol | 0.1 |
| Formaldehyde | 0.05 |

information was included for the styrenes. Rate constants were 15.1 and $48 \times 10^9$ liter/mole-sec for propene, and 1,3-butadiene, respectively. Since benzene is more effective than alkyl groups in stabilizing radicals, reaction rates of greater than $50 \times 10^9$ liter/mole-sec are reasonable estimates for the rate constants.

Relatively little information was found from which to delineate reaction products of the styrenes or α-methylstyrene in photochemical smog chambers. If one can safely judge from products of aliphatic olefins, then products are expected to include peroxides, formaldehyde, benzaldehyde from styrene and acetophenone from α-methylstyrene.

### 5. Miscellaneous Reactions

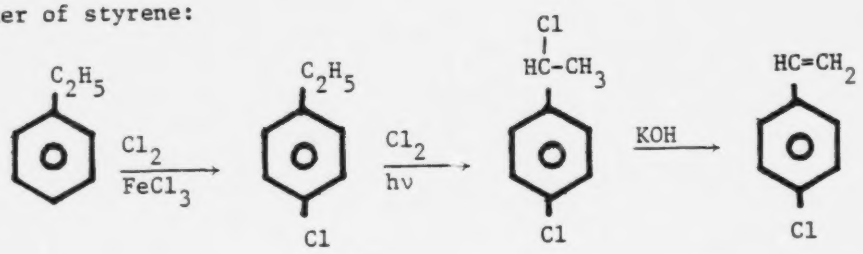
All aromatic compounds can be reduced by catalytic hydrogenation at high temperature and pressure. Under such conditions ethylbenzene forms ethylcyclohexane. The vinylic benzenes undergo hydrogenation of their unsaturated side chains much more readily than the aromatic ring. It is, therefore, quite easy to produce ethylbenzene by hydrogenation of styrene under appropriate reaction conditions.

Like other alkyl benzenes, ethylbenzene undergoes electrophilic aromatic substitution (Friedel-Crafts reaction), a technique for placing other alkyl substituents on the ring system. A typical example is shown in Table 9.

Free radical substitution at the side chain of alkyl benzenes occurs in the presence of light. In the absence of light, but with the aid of a suitable catalyst, electrophilic substitution occurs on the benzene ring.

Acetophenone is produced by the catalytic oxidation of ethylbenzene in air, the first step in a former commercial method for the preparation of styrene (Hornibrook, 1962). The styrene is then formed by hydrogenation of the acetophenone to 1-phenylethanol, followed by catalytic dehydration. Although the styrene yields for this process are good, they are not quite as good as for the direct dehydrogenation of ethylbenzene.

A combination of the reactions discussed thus far may form the basis for the preparation of p-chlorostyrene, another commercially important copolymer of styrene:



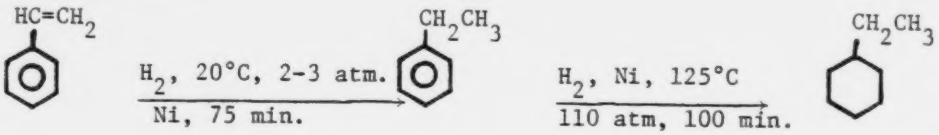
Alkenes readily undergo addition of halogens, hydrogen halides, etc. to the double bond. In vinyl benzenes, the double bonds of the alkenes are even more reactive to such additions than aliphatic alkenes. Some examples are given in Table 9.

The most important commercial reaction of styrene monomers is polymerization. Styrene monomers polymerize by addition polymerization, so called because the monomers join together without the formation of any by-products. Addition polymerizations proceed by a mechanism involving the initial formation of a highly reactive species such as a free radical or ion which attacks the monomer molecule forming a new free radical or ion which in turn attacks other monomer molecules, adding them to the growing chain. The acid catalyzed polymerization of styrene is illustrated in Table 9. Under environmental conditions styrene monomer molecules would most likely be easily oxidized or hydrolyzed. However, if enough of them are present in a confined area, such as right after

Table 9. Miscellaneous Reactions of Styrene Monomers and Ethylbenzene (Morrison and Boyd, 1974)

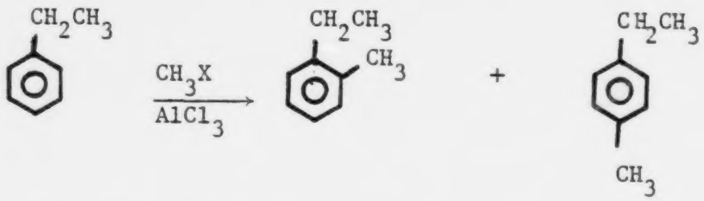
---

1. Hydrogenation



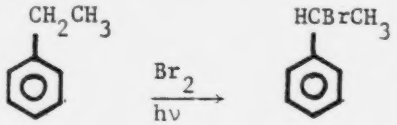
HC=CH2
H2, 20°C, 2-3 atm.
Ni, 75 min.
CH2CH3
H2, Ni, 125°C
110 atm, 100 min.
CH2CH3

2. Electrophilic Aromatic Substitution



CH2CH3
CH3X
AlCl3
CH2CH3
CH3
+
CH2CH3
CH3

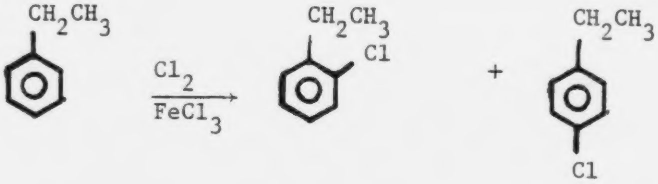
3. Free Radical Substitution in Side Chain



CH2CH3
Br2
hν
HCBrCH3

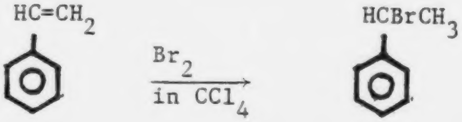
(only product)

4. Electrophilic Substitution



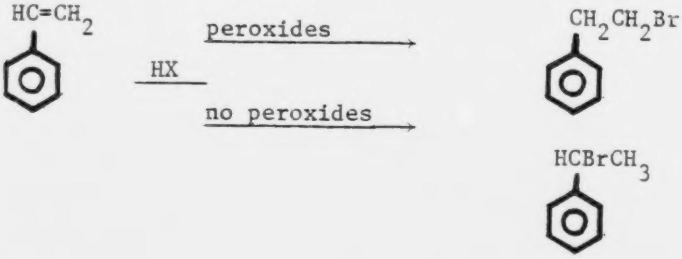
CH2CH3
Cl2
FeCl3
CH2CH3
Cl
+
CH2CH3
Cl

5. Addition to Double Bond



HC=CH2
Br2
in CCl4
HCBrCH3

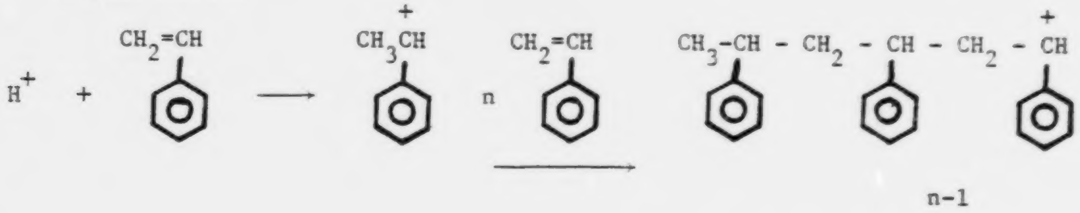
6. Addition of HX



HC=CH2
HX
peroxides
no peroxides
CH2CH2Br
HCBrCH3

Table 9. Miscellaneous Reactions of Styrene Monomers and Ethylbenzene (Morrison and Boyd, 1974) (Cont'd)

7. Polymerization[a]



---

[a] Brescia *et al.*, 1974

a catastrophic spill, polymerization could be a significant reaction under certain conditions (e.g., soil could catalyze polymerization).

# II. Environmental Exposure Factors

## A. Production Aspects

### 1. Quantity Produced, Imported and Exported

Table 10 lists the U.S. production of ethylbenzene, styrene, α-methylstyrene, and divinylbenzene for the ten year period 1967 to 1976. The production quantities of ethylbenzene have been estimated by assuming that nearly all of the ethylbenzene production (minus export quantities) is used to make styrene. Since most of the ethylbenzene producers also produce styrene, it is not uncommon for the ethylbenzene production units to be tied on-stream to the styrene production units to avoid storage and other costs which may be involved. The ethylbenzene production excluding the continuous streams used in some styrene production is also listed in Table 10. Based upon 1974 to 1976 figures, approximately 18 to 20% of the total annual ethylbenzene production is used in continuous styrene processes.

The most recent available production figure for divinylbenzene is 3.4 million pounds in 1972 (USITC, Annual a). However, most of the divinylbenzene production is consumed in the production of styrene-divinylbenzene polymers used for ion-exchange resins. Typically, these resins contain 8% divinylbenzene and were produced in quantities of 70 to 75 million pounds in 1974 and 1975 (Soder, 1977). Therefore, the 1974 and 1975 production volumes for divinylbenzene can be estimated at about 5.6 million pounds annually.

Imports and exports of ethylbenzene, styrene, and α-methylstyrene are given in Table 11. There is no data available which indicates that divinylbenzene is either imported or exported. As can be seen from Table 11, imports of ethylbenzene and α-methylstyrene are virtually insignificant as

Table 10. U.S. Production of Ethylbenzene, Styrene, α-Methylstyrene, and Divinylbenzene

(Quantities in Millions of Pounds)

| | Ethylbenzene[*] | Styrene[**] | α-Methylstyrene[**] | Divinylbenzene[**] | Ethylbenzene[**] (excluding styrene continuous streams) |
|---|---|---|---|---|---|
| 1976 | 7,200 | 6,301 | 61.4 | n.a. | 6,127 |
| 1975 | 5,500 | 4,673 | 29.9 | n.a. | 4,822 |
| 1974 | 7,090 | 5,956 | 57.2 | n.a. | 6,048 |
| 1973 | 7,100 | 5,975 | 52.5 | n.a. | 5,688 |
| 1972 | 7,080 | 5,941 | 37.4 | 3.4 | 5,676 |
| 1971 | 5,600 | 4,682 | 20.8 | 2.9 | 4,984 |
| 1970 | 5,380 | 4,335 | 19.1 | 3.2 | 4,827 |
| 1969 | 5,750 | 4,648 | n.a. | 3.3 | 4,907 |
| 1968 | 4,550 | 3,698 | n.a. | 2.8 | 4,034 |
| 1967 | 4,000 | 3,278 | 15.9 | 2.7 | 3,347 |

[*] SRC Estimates

[**] USITC, Annual a

Table 11. Imports and Exports of Ethylbenzene, Styrene, and α-Methylstyrene

(Quantities in Millions of Pounds)

| | Ethylbenzene | | Styrene | | α-Methylstyrene | |
|---|---|---|---|---|---|---|
| | Imports[1] | Exports[2] | Imports[1] | Exports[3] | Imports[1] | Exports[4] |
| 1976 | --- | 143 | 24.8 | 952 | --- | 12-24 |
| 1975 | 0.9 | 84 | 6.7 | 574 | 0.01 | n.a. |
| 1974 | 6.1 | 138 | 60.9 | 623 | --- | 12 |
| 1973 | 5.6 | 185 | 30.8 | 575 | --- | --- |
| 1972 | 0 | 207 | 21.0 | 661 | --- | --- |
| 1971 | 0 | 225 | 0.5 | 369 | --- | --- |
| 1970 | 0 | 405 | 9.5 | 568 | --- | --- |
| 1969 | 3.8 | 435 | 13.6 | 832 | --- | --- |
| 1968 | 0.7 | 320 | 9.4 | 538 | --- | --- |
| 1967 | 0 | 250 | 16.6 | 436 | --- | --- |

---

[1] USITC, annual b

[2] Paul and Soder, 1977

[3] Soder, 1977; U.S. Bureau of the Census, 1976

[4] SRC estimate

compared to domestic production while imports of styrene are historically less than 1% of domestic production. Exports are much more important; historically, 9 to 18% of the styrene produced and 1.5 to 7% of the ethylbenzene produced domestically is exported. Exports of α-methylstyrene range from 20 to 40% of production (Chem. Prof., 1977c).

### 2. Producers, Production Sites, and Major Distributors

The current producers of ethylbenzene, styrene, α-methylstyrene, and divinylbenzene are listed in Table 12 along with their respective production sites and available production capacities. Individual capacities are not available for divinylbenzene; however, the total current industry capacity for divinylbenzene can be estimated to be approximately 7 to 8 million pounds annual, based upon current production estimates of 6 million pounds annually (SRC estimates).

Former producers of α-methylstyrene, as late as 1975, were Dow Chemical (Midland, Mich.) and Union Carbide (Bound Brook, N.J.); they are not producing α-methylstyrene at this time.

In general, the major distributors of these chemicals are the producers. Other major distributors are listed in Table 13. From Table 12 it must be noted, however, that most of the production of ethylbenzene and styrene is captively consumed by the producers. For example, more than 90% of the ethylbenzene production is captively consumed while approximately 50% of the styrene production is captively consumed.

Figure 2 is a map which shows the geographical location of the production sites for ethylbenzene, styrene, α-methylstyrene, and divinylbenzene. The cluster of production sites in Texas and Louisiana is notable.

Table 12. Producers of Ethylbenzene, Styrene, α-Methylstyrene, and Divinylbenzene*

| Producer | Location | Ethylbenzene Total Annual Capacity (Millions of Pounds) | Remarks |
|---|---|---|---|
| Amoco Chem. Corp. | Texas City, Tex. | 985 | captive for styrene |
| ARCO/Polymers Inc. | Port Arthur, Tex. | 500 | captive for styrene |
| | Houston, Tex. | 135 | distilled from mixed xylenes |
| Charter Oil Co. | Houston, Tex. | 40 | distilled from mixed xylenes; all is sold |
| Cosden Oil & Chem. Co. | Big Spring, Tex. | 45 | distilled from mixed xylenes; captive for styrene |
| Cos-Mar, Inc. | Carville, La. | 1520 | captive for styrene |
| Dow Chem. USA | Freeport, Tex. | 1865 | captive for styrene |
| | Midland, Mich. | 550 | captive for styrene |
| El Pasa Natural Gas Co. | Odessa, Tex. | 275 | partly captive for styrene |
| Foster Grant Co. | Baton Rouge, La. | 1160 | captive for styrene |
| Gulf Oil Corp. | Donaldsville, La. | 615 | captive for styrene |
| Joc Oil Co. | Houston, Tex. | 30 | extracted from waste styrene tars; all is sold |
| Monsanto Co. | Alvin, Tex.<br>Texas City, Tex. | 1700 | 33 million lbs/yr distilled from mixed xylenes; captive for styrene |
| Oxirane Chem. Co. | Channelview, Tex. | 1160 | came on-stream in mid-1977 |
| Phillips Petroleum Co. | Phillips, Tex. | n.a. | research grade |
| Styrochem Corp. | Penuelas, P.R. | 160 | distilled from mixed xylenes; all is sold |
| Sun Oil Co. | Corpus Christi, Tex. | 95 | 33 million lbs/yr distilled from mixed xylenes; captive for styrene |
| Tenneco, Inc. | Chalmette, La. | 35 | distilled from mixed xylenes; all is sold |
| Union Carbide | Seadrift, Tex. | 340 | captive for styrene |
| | TOTAL | 11,210 | |

Table 12. Producers of Ethylbenzene, Styrene, α-Methylstyrene, and Divinylbenzene (Cont'd)*

| Producer | Location | Styrene Total Annual Capacity (Millions of Pounds) | Remarks |
|---|---|---|---|
| Amoco Chem. Corp. | Texas City, Tex. | 840 | 40% captive for polystyrene mfg. |
| ARCO/Polymers, Inc. | Kobuta, Pa. | 440 | captive for polystyrene & SB latex |
|  | Houston, Tex. | 120 | all may be sold |
| Cosden Oil & Chem. Co. | Big Spring, Tex. | 90 | captive for polystyrene |
| Cos-Mar, Inc. | Carville, La. | 1300 | partly captive |
| Dow Chem. USA | Freeport, Tex. | 1450 | captive for Dow plants at eight U.S. locations |
|  | Midland, Mich. | 400 |  |
| El Pasa Natural Gas Co. | Odessa, Tex. | 150 | no captive use; to be increased to capacity of 240 million lbs in 1978 |
| Foster Grant Co. | Baton Rouge, La. | 990 | 50% captive for polystyrene |
| Gulf Oil Corp. | Donaldsonville, La. | 600 | no captive use |
| Monsanto Co. | Texas City, Tex. | 1500 | 35% captive for polystyrene, ABS, SAN at four U.S. locations |
| Oxirane Chem. Co. | Channelview, Tex. | 1000 | came on-stream in mid-1977; no captive use |
| Sun Oil Co. | Corpus Christi, Tex. | 80 | no captive use |
| Union Carbide | Seadrift, Tex. | 300 | partly captive |
|  | TOTAL | 9,260 |  |

Table 12. Producers of Ethylbenzene, Styrene, α-Methylstyrene, and Divinylbenzene[*] (Cont'd)

| Producer | Location | | α-Methylstyrene<br>Total Annual Capacity (Millions of Pounds) | Remarks |
|---|---|---|---|---|
| Allied Chem. Corp. | Frankford, Pa. | | 24 | |
| Clark Oil & Refining | Blue Island, Ill. | | 5 | |
| Georgia-Pacific Corp. | Plaquemine, La. | | 10 | |
| Getty Oil Co. | El Dorado, Kans. | | 2 | |
| U.S. Steel Corp. | Haverhill, Ohio | | 15 | |
| Union Carbide | Bound Brook, N.J. | | 8 | |
| | | TOTAL | 64 | capacities are somewhat flexible |
| | | | Divinylbenzene | |
| ARCO/Polymers, Inc. | Beaver Valley, Pa. | | n.a. | |
| Dow Chem. USA | Midland, Mich. | | n.a. | |
| Foster Grant Co. | Baton Rouge, La. | | n.a. | |

---

[*] Sources: SRI, 1977; Soder, 1977; Paul and Soder, 1977; Chem. Prof., 1977c

Table 13. Major Distributors of Styrene, Ethylbenzene, α-Methylstyrene, and Divinylbenzene (Chem. Mark. Reporter, 1977b; Chemical Week, 1977)

| | |
|---|---|
| Divinylbenzene | |
| Fallek Chemical Corp. | New York, N.Y. |
| α-Methylstyrene | |
| Jonas Chemical Corp. | New York, N.Y. |
| Sattva Trading Co., Inc. | Stamford, Conn. |
| Ethylbenzene | |
| Carbonit America, Inc. | New York, N.Y. |
| Esselen Associates, Inc. | Stamford, Conn. |
| Montedison USA, Inc. | New York, N.Y. |
| Stanalchem, Inc. | New York, N.Y. |
| Stinnes Oil & Chemical Co. | New York, N.Y. |
| Fallek Chemical Corp. | New York, N.Y. |
| Helm Houston Chem. Corp. | Houston, Tex. |
| Styrene Monomer | |
| Agrimet, Inc. | New York, N.Y. |
| Esselen Associates, Inc. | Stamford, Conn. |
| Fallek Chemical Corp. | New York, N.Y. |
| HCI Chemicals (U.S.A.) | Houston, Tex. |
| Helm Chemical Corp. | New York, N.Y. |
| Holtrachem, Inc. | Natick, Mass. |
| Hoosier Solvents & Chemicals Corp. | Indianapolis, Ind. |
| International Commodities Export Co. | New York, N.Y. |
| Kah Chemical Co. | Wellesley Hills, Mass. |
| George Mann & Co., Inc. | Providence, R.I. |
| Montedison USA | New York, N.Y. |
| Morgan Chemicals, Inc. | Williamsville, N.Y. |
| Pioneer Salt & Chemical Co. | Philadelphia, Pa. |
| Prillaman Chemical Corp. | Martinsville, Va. |
| Southland Solvents & Chemical Co. | Jamestown, N.C. |
| Stanalchem, Inc. | New York, N.Y. |
| Stinnes Oil & Chemical Co. | New York, N.Y. |
| T.R. America, Inc. | New York, N.Y. |
| White Cross Laboratories, Inc. | New York, N.Y. |

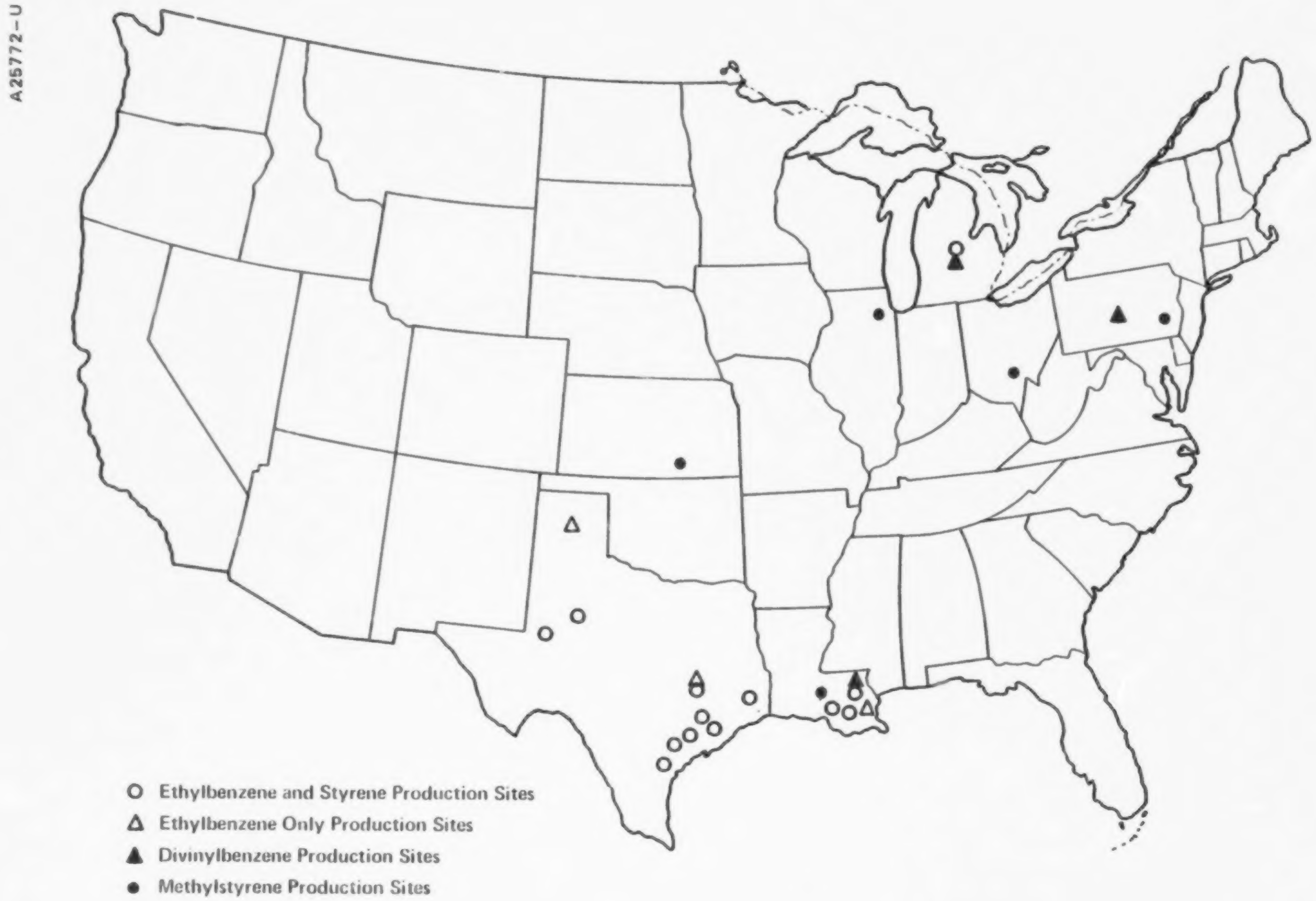

A25772-U
○ Ethylbenzene and Styrene Production Sites
△ Ethylbenzene Only Production Sites
▲ Divinylbenzene Production Sites
● Methylstyrene Production Sites

Figure 2. Geographical Location of Production Sites for Ethylbenzene, Styrene, Divinylbenzene, and α-Methylstyrene

## 3. Current Production Methods

### a. Ethylbenzene

#### (1) Liquid-Phase Benzene Alkylation

The most widely used process in the U.S. for the production of ethylbenzene is the liquid-phase. Friedel-Crafts alkylation of benzene with ethylene using aluminum chloride as catalyst with ethyl chloride or hydrogen chloride as promoters (Faith *et al.*, 1975; McDowell, 1978; Coulter *et al.*, 1969). The process is schematically shown in Figure 3.

The benzene used is known as "styrene grade," which defines a benzene with a maximum boiling range of 1°C and a minimum freezing point of 5.3°C (dry); this ordinarily corresponds to a purity slightly above 99%. The purity of the ethylene is not a prime consideration, except that it must be free of acetylene, other unsaturates, and moisture. In general, ethylene of at least 90% purity is used.

The alkylation process is carried out in a brick-lined steel tower or a glass-lined reactor operating at the boiling point of the reaction mixture (80 to 100°C at atmospheric pressure). The conventional reactor, which operates at about atmospheric pressure, is filled to approximately 35 feet with the liquid reactants which overflow through a line near the top. Ethylene is introduced at the bottom of the reactor, as is the fresh benzene, recycle benzene, recycle polyethylbenzenes, and the catalyst complex. The catalyst complex is an oily, reddish-brown addition compound consisting of 25 to 30% aluminum chloride chemically combined with 70 to 75% of various alkylator product compounds.

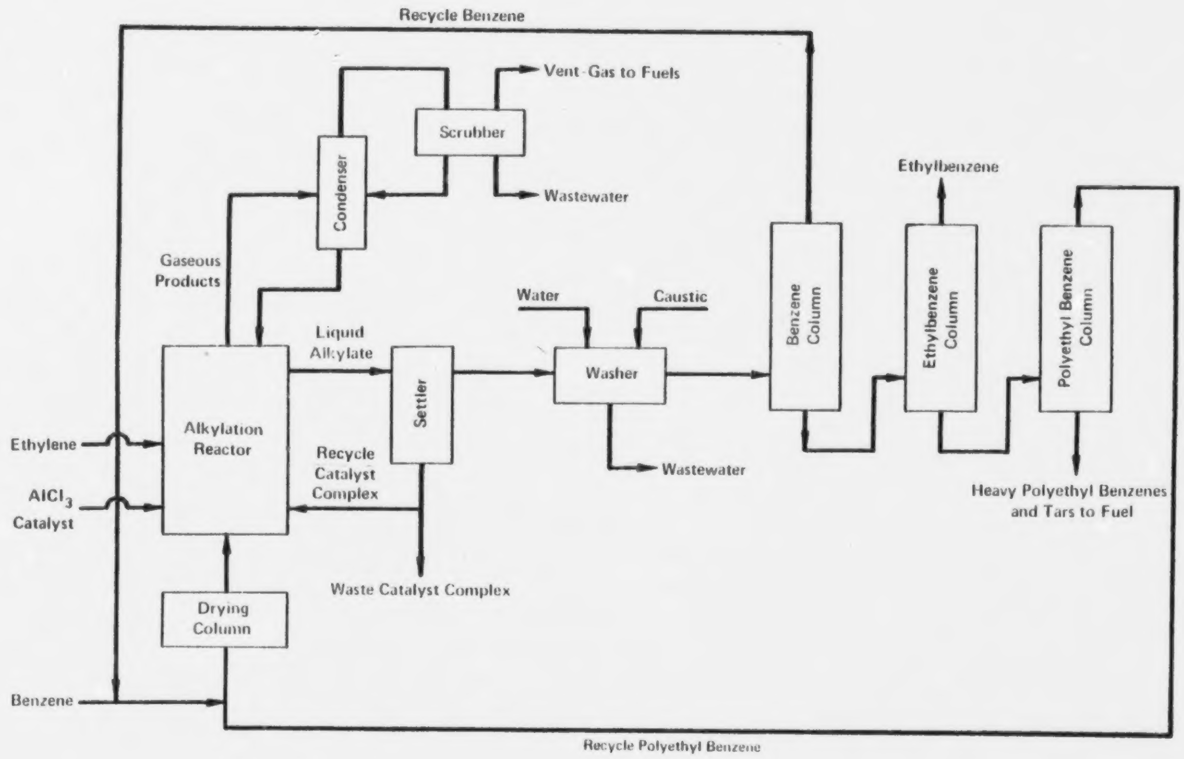
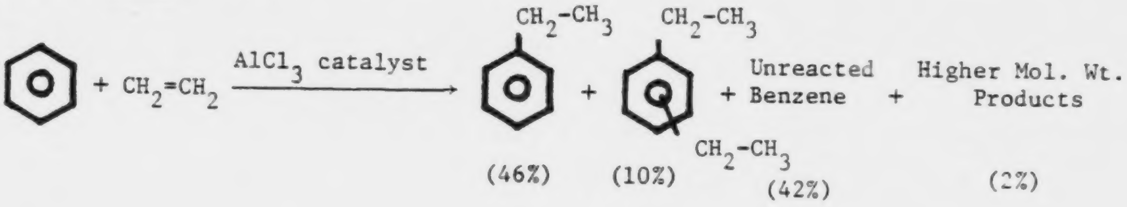

C25773-U
Recycle Benzene
Vent-Gas to Fuels
Scrubber
Condenser
Wastewater
Gaseous Products
Ethylbenzene
Water
Caustic
Liquid Alkylate
Washer
Benzene Column
Ethylbenzene Column
Polyethyl Benzene Column
Ethylene
Alkylation Reactor
Settler
Recycle Catalyst Complex
Wastewater
$AlCl_3$ Catalyst
Heavy Polyethyl Benzenes and Tars to Fuel
Waste Catalyst Complex
Drying Column
Benzene
Recycle Polyethyl Benzene

Figure 3. Ethylbenzene Manufacture Via Benzene Alkylation (Ethylene) (Adapted from Faith et al., 1975; Coulter et al., 1969)

The general chemical reaction equation which describes a single pass of reactants through the alkylation reactor is the following (Coulter *et al.*, 1969):



The overall yield of benzene to ethylbenzene averages 95.5%, whereas that of ethylene to ethylbenzene averages 96.8% (Faith *et al.*, 1975).

The gaseous products, unreacted ethylene, small amounts of benzene, hydrogen chloride, and the inerts (that were introduced with the ethylene) leave the top of the reactor and enter a condenser from which recovered benzene flows back to the alkylator. The off-gas is scrubbed for final benzene recovery, using recycle polyethylbenzenes as absorbent, and then is washed with water for the removal of HCl before venting or being compressed for use as fuel (Coulter *et al.*, 1969).

The liquid products from the alkylator (ethylbenzene, unreacted benzene, diethyl- and polyethylbenzenes) are cooled and passed through a settler where the catalyst complex is removed and returned to the alkylator. The alkylate is then washed with water, which breaks any residual complex, and scrubbed with 20% caustic to neutralize the acidic constituents, after which it is separated into components in a series of distillation columns. The first column removes the benzene for recycle to the alkylator; the second column removes the ethylbenzene product; and the third column separates the lighter polyethylbenzenes for recycle to the alkylator. The lighter polyethylbenzenes can be chemically broken down to ethylbenzene by reaction with benzene in the reactor. The bottoms product of the third column are heavy polyethylbenzenes and tars, which are burned as fuels.

One operating precaution is to remove the diethylbenzene from the monoethylbenzene as completely as possible. If this is not done, divinylbenzene will be formed in subsequent dehydrogenation steps to styrene and, on distillation can polymerize with styrene to a cross-linked polymer which is very hard to remove. Isopropylbenzene (cumene) should also be removed, if formed, to prevent contamination of the styrene with α-methylstyrene and unreacted cumene (Coulter _et al_., 1969).

In addition to the conventional Friedel-Crafts alkylation process (also known as the Cosden-Carbide-Badger process) described above, two recent benzene alkylation processes have been commercially developed in the past several years. Their main advantage over the conventional alkylation is a substantial saving in the fuel costs. These processes are the Monsanto-Lummus process and the Mobil-Badger process.

## Monsanto-Lummus Process

The Monsanto-Lummus process is also based upon the alkylation of benzene with ethylene; however, it does not utilize a recycling catalyst complex. Monsanto found that the conventional catalyst phase is not only unnecessary, but actually harmful in obtaining maximum yields (Oil and Gas J., 1976b). The Monsanto-Lummus process uses an aluminum chloride catalyst which is continuously removed and replenished with no recycle. The removed catalyst is converted into an aqueous aluminum chloride solution as a by-product for water treatment and other applications (Chemical Week, 1976). This eliminates the problem of catalyst discharge.

The Monsanto-Lummus process has demonstrated commercial capability at Monsanto's 1.7 billion pounds per year ethylbenzene production facility in Texas City, Texas which began using the process in 1974. Yields of 99% and on-stream times of 99% were recorded in the first year of operation (Chemical Week, 1975).

## Mobil-Badger Process

The Mobil-Badger process uses a solid, non-Friedel-Crafts catalyst to alkylate the benzene with ethylene. The catalyst, designated APEB, is a proprietary development of Mobil; however, patent literature indicates that the catalyst may be Mobil's ZSM-5, a crystalline aluminosilicate zeolite with a unique X-ray diffraction pattern. A related compound, ZSM-12, is also a possibility (Chemical Week, 1975).

In the Mobil-Badger process, the alkylation occurs above 700°F and at 200 to 400 psi, which are conditions differing from the conventional process. The Mobil-Badger process makes the following environmental safety claims (Dwyer et al., 1976): First, the catalyst presents no hazards or waste-disposal problems and is environmentally inert; second, no process streams are produced that require treatment. Besides ethylbenzene, the only streams are the light vent gas and heavy residues, which are used as fuels.

Commercial capability of this process was demonstrated in 1975 in a 40 million pounds per year plant operated at the Foster-Grant ethylbenzene complex in Baton Rouge, La. (Chemical Week, 1976).

### (2) Alkar Vapor-Phase Benzene Alkylation

The only vapor-phase ethylbenzene production process commercially used is the high pressure UOP (Universal Oil Products) Alkar process, which uses a boron trifluoride catalyst on an inert base. This process was designed to operate on refinery gas streams containing 8 to 10% ethylene. Feedstocks of 5 to 100% ethylene may be used. A simplified flowsheet of the Alkar process is shown in Figure 4.

Fresh benzene is mixed with recycle benzene and ethylene and, after heating to reactor temperature, are fed into the fixed-bed alkylator along with the boron trifluoride-supported catalyst. Reaction conditions are reportedly 150 to 250°C and 400 to 700 psi (Faith et al., 1975). The high-pressure effluent is then flashed and fed into the benzene recycle column where the benzene is recovered as overhead product. The bottoms become the feed to the second column, where the product ethylbenzene is separated from the polyalkylbenzenes. Most of the polyalkylbenzenes are recycled to a separate dealkylator along with the necessary benzene for conversion back to ethylbenzene. The dealkylator effluent is then combined with the alkylator effluent for flashing. The yield of ethylbenzene is reportedly quantitative with respect to benzene after transalkylation of the polyalkylbenzenes (Coulter et al., 1969). A small purge of bottoms from the ethylbenzene column is required for removal of traces of other alkylates formed from propylene (cumene, for example) and acetylene in the feed of ethylene.

The Alkar process offers the advantage of less corrosion than the conventional aluminum chloride liquid-phase process; however, the cost of heating fuels is substantially higher making the Alkar process unattractive with respect to conventional processes.

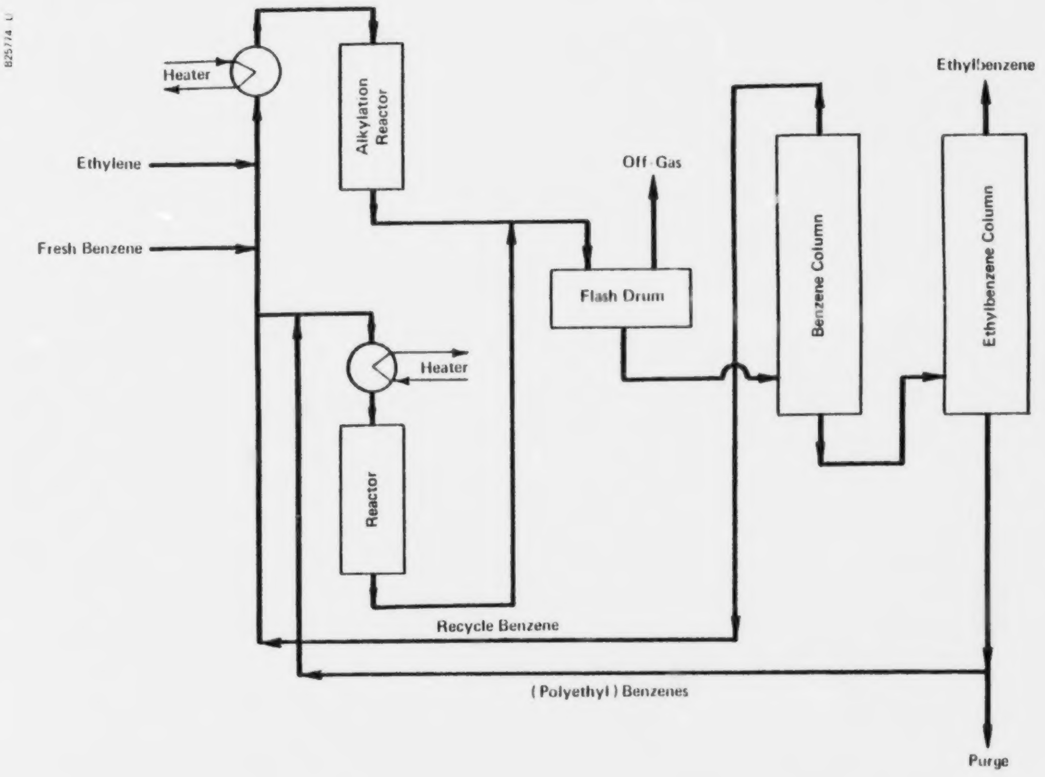

825774 U
Heater
Alkylation Reactor
Ethylene
Fresh Benzene
Heater
Reactor
Flash Drum
Off-Gas
Benzene Column
Ethylbenzene
Ethylbenzene Column
Recycle Benzene
(Polyethyl) Benzenes
Purge

Figure 4. Alkar Ethylbenzene Process (Adapted from Coulter *et al.*, 1969)

### (3) Fractionation of Ethylbenzene from Mixed Xylene Streams

This process was introduced commercially by Cosden in 1957 and is schematically shown in Figure 5. Mixed xylenes occur naturally, but only in small quantities in crude petroleum; about 0.9% by volume (Carlson, 1975). Direct separation cannot be economically justified. However, in the initial distillation of crude petroleum into component streams, a naphtha stream is obtained which not only contains the natural mixed xylenes, but is rich in naphthlenes (alicyclics) and paraffins. This naphtha stream is catalytically reformed to produce a high-octane gasoline rich in aromatics. Mixed xylenes are produced, along with benzene and toluene, during the catalytic reforming, and are taken-off in a stream known as BTX (benzene-toluene-xylene). This BTX stream is sent to a liquid-liquid extractor to separate the benzene and toluene from the mixed xylenes. The mixed xylene stream coming from the extractor will vary in composition; however, a typical composition would be ethylbenzene 20%, *m*-xylene 40%, *o*-xylene 20%, and *p*-xylene 20% (Carlson, 1975).

The mixed xylene stream is sent to a fractionation system containing three large columns in series and operated at high reflux rates. Ethylbenzene is separated from its nearest xylene isomer, *p*-xylene, which boils 3.9°F higher than ethylbenzene. The purity of the ethylbenzene which is obtained, 99%+, is particularly important because the product styrene purity is determined by the purity of the ethylbenzene.

The U.S. production of ethylbenzene by distillation from mixed xylene streams is estimated to have been the following (Carlson, 1975; SRC estimates).

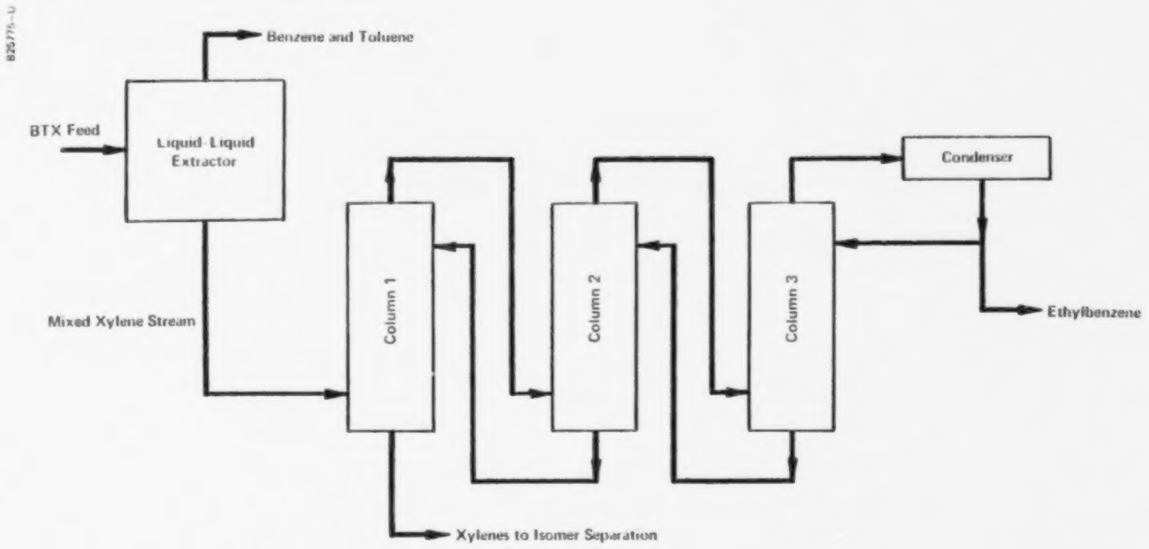

825775-U
Benzene and Toluene
BTX Feed
Liquid-Liquid Extractor
Mixed Xylene Stream
Column 1
Column 2
Column 3
Condenser
Ethylbenzene
Xylenes to Isomer Separation

Figure 5. Ethylbenzene Via Mixed Xylene Fractionation (Adapted from Stobaugh, 1965; Coulter et al., 1969; Carlson, 1975; Cier, 1970)

| Year | Quantity (million lbs) | Year | Quantity (million lbs) |
|---|---|---|---|
| 1976 | 300 | 1971 | 330 |
| 1975 | 270 | 1970 | 325 |
| 1974 | 365 | 1969 | 455 |
| 1973 | 350 | 1968 | 450 |
| 1972 | 345 | 1967 | 395 |

Based upon the total ethylbenzene production estimate of 7,200 million pounds in 1976 (Table 10), the ethylbenzene obtained from the fractionation of mixed xylenes accounted for only 4% of the total production; the other 96% of production came from benzene alkylation.

It is believed that due chiefly to the high energy requirements necessary to fractionate ethylbenzene from mixed xylenes, it is unlikely that there will be any large increases in ethylbenzene fractionation capacity.

> "The recovery of natural ethylbenzene is usually carried out as an adjunct to the recovery of the xylene isomers but this is not necessarily done. The ethylbenzene in the mixed xylenes can be isomerized to maximize ortho- and para-xylene recovery. It is probable that the isomerization technique will be used to an increasing extent. Thus, the isolation of ethylbenzene from mixed xylene streams may continue to decline at the same time that the isolation of the individual xylene isomers continues to increase" (Carlson, 1975).

#### (4) Extraction from Styrene Tars

Joc Oil Aromatics (a division of Joc Oil, Inc.) in Houston, Texas, treats waste tars from chemical plants. One treatment involves extraction of ethylbenzene from styrene tars. Capacity for ethylbenzene extraction is 30 million pounds per year (Paul and Soder, 1977).

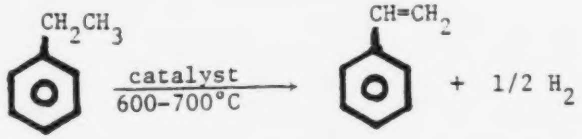
### b. Styrene

At present, most of the styrene produced in the U.S. is made by the dehydrogenation of ethylbenzene in vapor phase. However, in late 1977

Oxirane (Channelview, Texas) brought on-stream a plant which produces styrene as a co-product from propylene oxide manufacture.

### (1) Dehydrogenation of Ethylbenzene

Ethylbenzene is dehydrogenated to styrene by the following reaction, which is endothermic:



The above reaction is the desired selective reaction; however, various non-selective reactions will also occur. For example, benzene and toluene are produced in quantities which average 0.7% and 1.0% of reactor effluent, respectively (Faith _et al._, 1975). The purity of the ethylbenzene feed, which must be 99% or better, is of prime importance. Contaminants, such as diethylbenzene, will also be dehydrogenated and will produce products which form unwanted polymers.

A schematic of the general industry production method is given in Figure 6. Purified ethylbenzene is preheated, first with steam (to 160°C), and then by heat exchange (to 520°C) with the effluent reactor products. Superheated steam (710°C) and ethylbenzene vapors are continuously mixed and fed into a reactor at a ratio of 2.6 kg steam/kg ethylbenzene. The reactor contains a selective fixed-bed dehydrogenation catalyst such as zinc, chromium, iron, or magnesium oxide, on activated charcoal, aluminas, or bauxites. The catalyst operates continuously and has a production life of 1 to 2 years. At a catalyst temperature of about 630°C, resulting from the vapor-feed temperature, conversions of 35 to 40% per pass of reactants through the reactor may be realized. Usual overall yields of 90% ethylbenzene to styrene are realized.

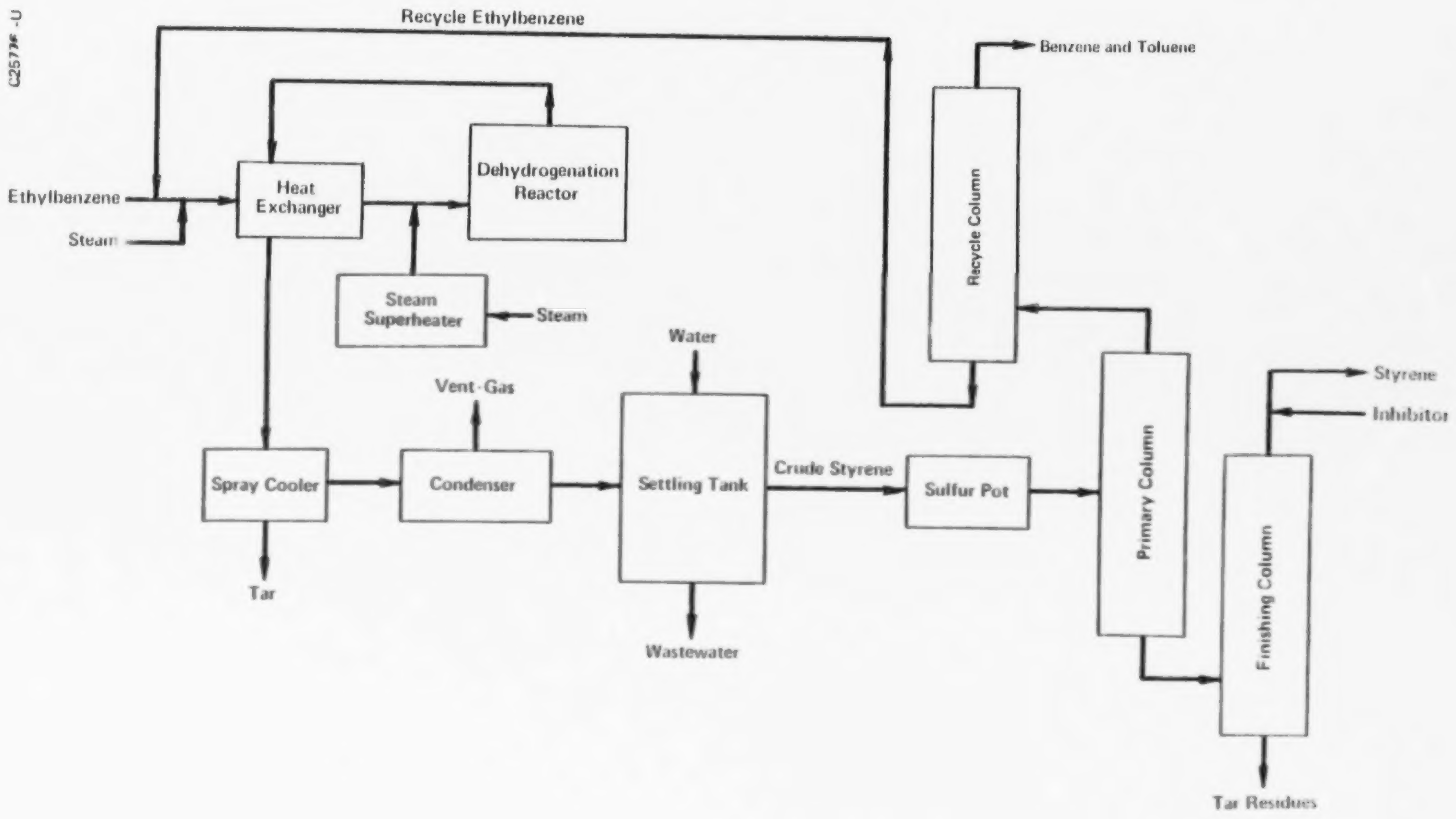

C2577* -U
Recycle Ethylbenzene
Benzene and Toluene
Ethylbenzene
Steam
Heat Exchanger
Dehydrogenation Reactor
Steam Superheater
Steam
Recycle Column
Water
Vent-Gas
Spray Cooler
Condenser
Settling Tank
Crude Styrene
Sulfur Pot
Primary Column
Finishing Column
Styrene
Inhibitor
Tar
Wastewater
Tar Residues

Figure 6. Styrene Production Via Ethylbenzene Dehydrogenation (Adapted from Faith et al., 1975; Austin, 1974; Coulter et al., 1969)

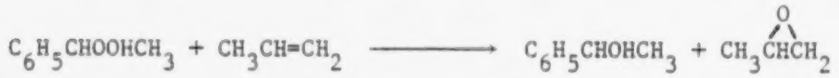
The reaction products leave the top of the reactor at about 565°C and are cooled by the influent ethylbenzene in heat exchangers. A spray-type cooler lowers the product temperature to about 105°C and condenses out some of the tars which may contain some stilbene and biphenyl. A final condenser liquifies the steam (styrene, toluene, and benzene) while the vent gases containing hydrogen, carbon monoxide, carbon dioxide, and lower aliphatic hydrocarbons are sent to a refrigerated recovery system. The condensed materials pass to a settling tank, where the hydrocarbons are decanted and the water is discharged to a disposal system.

The crude styrene, of average composition 37% styrene, 61% ethylbenzene, 1.0% toluene, 0.7% benzene, and 0.3% tars, is passed through a pot containing sulfur or some other polymerization inhibitor and is then fed to a vacuum column system. The overhead from a primary fractionating column is fractionated to separate the ethylbenzene, which is recycled, from the benzene and toluene, which are separated by distillation. The bottoms from a primary fractionating column are distilled to obtain the styrene product. A polymerization inhibitor, usually TBC (tert-butylcatechol), is added at the top of the column to prevent the styrene from polymerizing. The tar residue discharged from the finishing column bottom is sometimes buried, but Dow Chemical (Burgess, 1978) recommends using it for fuel. Union Carbide has just submitted an 8e notice to EPA under TSCA indicating that these polyethylated benzene tails "appear to be unequivocally highly carcinogenic in mice" (Toxic Materials News, 1978). The distilled styrene passes to receivers, where more inhibitor (TBC) is added to bring its concentration to 10 ppm. The finished material is refrigerated below 20°C and loaded to insulated tank cars for shipment (Faith *et al*., 1975; Austin, 1974; Coulter *et al*., 1969).

(2) Co-Product with Propylene Oxide

In late 1977, Oxirane Corp. brought into production a plant which makes styrene by the following method (Soder, 1977):

$$\underset{\text{(ethylbenzene)}}{C_6H_5CH_2CH_3} + O_2 \longrightarrow \underset{\text{(ethylbenzene hydroperoxide)}}{C_6H_5CHOOHCH_3}$$



$$C_6H_5CHOOHCH_3 + \underset{\text{(propylene)}}{CH_3CH{=}CH_2} \longrightarrow \underset{\text{(methyl phenyl carbinol)}}{C_6H_5CHOHCH_3} + \underset{\text{(propylene oxide)}}{CH_3\overset{O}{\widehat{CHCH_2}}}$$

$$C_6H_5CHOHCH_3 \longrightarrow \underset{\text{(styrene)}}{C_6H_5CH{=}CH_2} + H_2O$$

Ethylbenzene is oxidized to its hydroperoxide which is then reacted with propylene to yield propylene oxide and co-product methyl phenyl carbinol. The carbinol is then dehydrated to styrene.

c. α-Methylstyrene

(1) By-Product from Cumene-Phenol Process

The purification of small amounts of α-methylstyrene formed as a by-product in the cumene-phenol process is the most important industrial source of the monomer. At present, this is the only commercial source of α-methylstyrene as Dow's process of dehydrogenating cumene to α-methylstyrene has been shut-down.

In the industrial process which converts cumene into phenol and acetone, α-methylstyrene represents about 1.7% of the total cumene conversion (Coulter et al., 1969). In order to recycle cumene in this oxidative process, it must be essentially free of α-methylstyrene. Therefore, the hydrocarbon streams from the reaction must be subjected to a series of fractional distillations to remove this unwanted material. At present, some phenol manufacturers employing the cumene process find it more economical to hydrogenate the α-methylstyrene back to cumene and convert it to more phenol and acetone. Others have chosen to install additional finishing facilities for the monomer and market the product.

### (2) Dehydrogenation of Cumene

Through 1975, Dow Chemical produced α-methylstyrene by direct dehydrogenation of cumene. In a typical operation, a mixture of three parts steam to one part cumene is passed rapidly over an iron oxide dehydrogenation catalyst at elevated temperatures. The crude dehydrogenation mixture consists of cumene and α-methylstyrene, as well as small amounts of benzene, toluene, ethylbenzene, and styrene. The economical operation of this process demands that all of these components be separated and purified for reuse; this is accomplished through a series of fractional distillations (Coulter *et al.*, 1969).

### d. Divinylbenzene

Divinylbenzene is manufactured by the dehydrogenation of mixed isomeric diethylbenzenes. The diethylbenzenes used in the manufacture of divinylbenzene are side products produced in the manufacture of ethylbenzene by the alkylation of benzene with ethylene. Normally, these higher alkylated products are separated and recycled for dealkylation in the ethylbenzene production process. However, it is a simple matter to retain some of the diethylbenzene stream for making divinylbenzene. This diethylbenzene stream, from a typical alkylation, will consist of a mixture of the three possible isomers of diethylbenzene in the proportions 9.4%:61.5%:29.1% (o, m, p, respectively) and some sec-butyl- and isobutylbenzenes, which are separated from the diethylbenzenes before cracking (Coulter et al., 1969).

Dehydrogenation of diethylbenzenes is accomplished in the following way:

> "Dehydrogenation of the three isomers is carried out in an apparatus very similar to that used for styrene. Preheated vapors of the hydrocarbons are mixed with superheated steam and passed over catalysts of mixed metal oxides at temperatures around 600°C. The presence of two ethyl groups on the aromatic ring greatly increases the number of possible products. The major portion of the reaction effluent consists of m- and p-divinylbenzene, the corresponding ethylvinyl compounds, and some unreacted diethylbenzene. Essentially all of the o-diethylbenzene is isomerized to naphthalene in the dehydrogenation process. Minor contaminants also found are benzene, toluene, vinyltoluenes, ethyltoluenes, xylenes, ethylbenzene, and styrene. The distillation and finishing of this mixture is an extremely sensitive procedure since divinylbenzene polymerizes very readily even at moderate temperatures. The finishing may be carried out in a series of three columns [as shown in Figure 7]. In the first column a rough separation of the monomers from the lighter materials is accomplished. Benzene, toluene, xylene, ethylbenzene, styrene, diethylbenzene, vinyltoluenes, ethyltoluenes, and some ethylvinylbenzenes are collected as distillates and subjected to further fractionation in column 2, where the lower-boiling materials are taken overhead to be sold as solvent or burned. It is impractical to recover styrene from this stream due to the likelihood of contamination with divinyl materials. The bottoms product of column 2, which is primarily diethylbenzene with some ethylvinylbenzene, is returned to the dehydrogenation reactor. Bottoms product from column 1, which contains most of the ethylvinylbenzene and the divinyl compounds plus some higher-boiling materials, is taken to column 3. Here, under a vacuum of 10-15 mm, a final distillation to remove the naphthalene and tars is carried out. Appropriate inhibitors are employed throughout this step to limit the polymerization of the monomers. For commercial production no attempt is made to further purify the monomer and it is generally sold as a mixture of components, chiefly divinylbenzene and ethylvinylbenzene. For most applications divinylbenzene is used in low concentrations as a crosslinking agent and additional purification is neither necessary nor desirable (Coulter et al., 1969)."

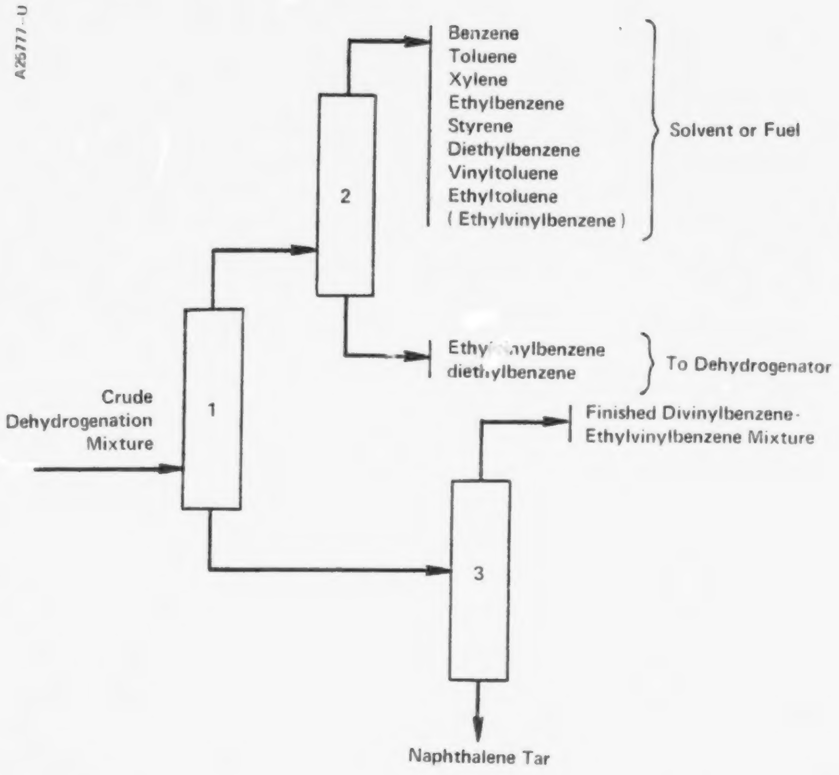

A25777-U
Benzene
Toluene
Xylene
Ethylbenzene
Styrene
Diethylbenzene
Vinyltoluene
Ethyltoluene
( Ethylvinylbenzene )
Solvent or Fuel
2
Ethylvinylbenzene
diethylbenzene
To Dehydrogenator
Crude Dehydrogenation Mixture
1
Finished Divinylbenzene-Ethylvinylbenzene Mixture
3
Naphthalene Tar

Figure 7. Finishing Distillations Used in the Manufacture of Commercial Divinylbenzene Monomer (Coulter et al., 1969)

### 4. Market Price and Trends

The market prices of ethylbenzene, styrene, α-methylstyrene, and divinylbenzene are listed in Table 14 for the period 1968 through the present.

#### a. Ethylbenzene

In addition to demand requirements, the market price of ethylbenzene is dependent upon the raw material costs of ethylene and benzene. In 1975, ethylbenzene production made up about 44% of the total benzene demand and 6% of the ethylene demand; these figures will rise to 50% of the benzene demand and 5% of the ethylene demand in 1985 (Chem. & Eng. News, 1977). Raw material benzene prices have been projected to rise from the 1975 level of $0.80 per gallon to $1.07 per gallon in 1980 and to $1.18 per gallon in 1985 (Chem. & Eng. News, 1977); however, more recent projections (Chem. & Eng. News, 1978) indicate that benzene prices may stabilize near $0.85 to 0.90 per gallon. Therefore, ethylbenzene prices will probably not rise significantly in the near future. Long term projections are not certain at this time.

Figure 8 diagrams ethylbenzene production by year and gives a graphical illustration of past market trends as well as future trends which have been forecasted. The historical growth of the ethylbenzene market has averaged about 9.3% per year (Chem. Prof., 1975). The decline in 1975 is attributed to the general economic recession during that year (Paul and Soder, 1977). Future growth is expected to average about 5% per year (Chem. Prof., 1975).

At the present time, 97% of the ethylbenzene production is used to manufacture styrene. Production increases or decreases of the two chemicals are directly related. Increased growth for ethylbenzene is dependent upon growth in the production of styrene-containing plastics.

Table 14. Market Prices of Ethylbenzene, Styrene, $\alpha$-Methylstyrene, and Divinylbenzene[*]

(Dollars per pound)

|  | Ethylbenzene | Styrene | $\alpha$-Methylstyrene | Divinylbenzene 50-60% | 20-25% |
|---|---|---|---|---|---|
| 1977 | .14 | .21 | .15 | .63 | .25 |
| 1976 | .14 | .20 | -- | .63 | .25 |
| 1975 | .09 | .19 | .12 | -- | -- |
| 1974 | .173 | .172 | .115 | -- | -- |
| 1973 | .05 | .07 | .06 | -- | -- |
| 1972 | .03 | .06 | .05 | .64 | -- |
| 1971 | .04 | .06 | .06 | .65 | -- |
| 1970 | .04 | .06 | .06 | .67 | -- |
| 1969 | .03 | .06 | .10 | .70 | -- |
| 1968 | .04 | .07 | .08 | .72 | -- |

---

[*] Source: USITC, Annual a; Chemical Marketing Reporter; Paul and Soder, 1977; Industrial Contacts

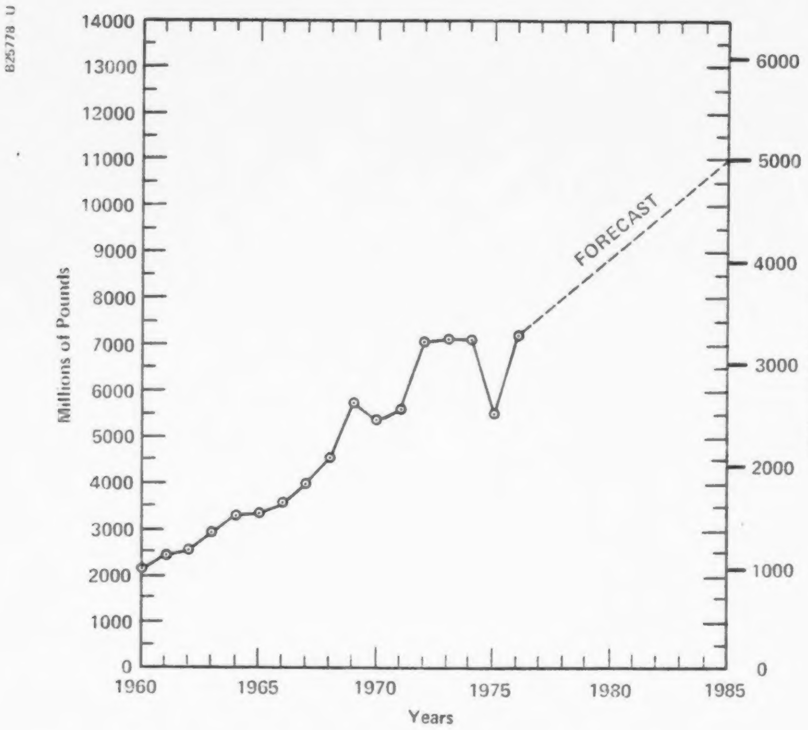


Figure 8. Ethylbenzene Production by Year

### b. Styrene

According to Charles V. Sleeth, Vice President of Marketing at Foster Grant Co. (Chem. & Eng. News, 1977), about 30% of the 1976 styrene capacity is in smaller, older, and less efficient plants. At current prices, Sleeth suspects that these plants' raw material and fuel costs are about 1.5 cents per pound of styrene higher than the larger modern plants. As industry is required to use higher priced fuels or other fuel sources, this cost disadvantage could increase to 4 cents per pound. Therefore, a number of older units may be expected to shut down in the next four or five years. Sleeth says that even for the newer and more efficient plants, fuel costs per pound could jump 2 cents to 2.5 cents.

Sleeth is predicting a growth rate of 6% per year to 1980 and 5% per year through 1985. The major factor affecting the long-range market is the rise in oil prices. Over the next few years, higher energy costs will lead to shifting patterns of demand. Sleeth thinks that these shifts will increase the demand for plastics, the major market for styrene; the trend for substituting plastics for other materials may even accelerate.

Chem. Prof. (1977d) is predicting a growth rate of 5% per year through 1981 for styrene. Currently, styrene is selling for $0.195 per pound which is down from the earlier 1977 prices of $0.21 per pound. This is primarily due to discounting of benzene used for raw material. As mentioned earlier, benzene prices may have temporarily stabilized near $0.80 per gallon. An increase in benzene prices, however, will cause styrene prices to rise.

### c. α-Methylstyrene

Historically (1967 to 1976), α-methylstyrene production has grown at a rate of 11% per year; future projections indicate that production will grow at an average rate of 6% per year through 1981 (Chem. Prof., 1977c). There is a large demand for α-methylstyrene both domestically and abroad, primarily for its use as an acrylonitrile-butadiene-styrene (ABS) additive for automotive products. These α-methylstyrene resins are useful in producing lighter, and thereby, more fuel efficient cars.

Growth will be supply-limited because α-methylstyrene is produced as a by-product of cumene-phenol operations which are experiencing low operating rates (Chem. Prof., 1977c). Exports of high-purity α-methylstyrene have been healthy thus contributing to a tight market domestically. These factors may be reflected in an upward trend in prices.

### d. Divinylbenzene

As compared to the other chemicals being studied in this report, divinylbenzene has been produced in only small quantities, 2.7 to 5.6 million pounds per year. However, the current outlook for the divinylbenzene market is quite good. Divinylbenzene is primarily used to make styrene-divinylbenzene resins which have applications in ion-exchange resins.

Average growth on the order of at least 8 to 10% per year for styrene-divinylbenzene resins is anticipated by most industry sources for 1976 to 1980 period, with some predicting average annual growth as high as 15%. Growth is expected to result primarily from increasing ion-exchange resin requirements of both municipal and industrial wastewater treatment facilities (Soder, 1977). By 1980, production of divinylbenzene may reach 9 to 11 million pounds, while by 1985, production may total 15 to 20 million pounds.

## 5. Quantity Produced as Contaminant of Other Materials

### a. Ethylbenzene and Styrene

Listed below is a summary of the quantities of ethylbenzene and styrene which exist as a contaminant or ingredient of materials:

| | Quantities in Millions of lbs./Year | |
|---|---|---|
| Source | Ethylbenzene | Styrene |
| Catalytic reformate | 9,400-10,000 | -- |
| Pyrolysis gasoline | 57-96 | 228-342 |
| Polymers & resins | 2-3 | 4-5 |

As explained in Section II. A. 3. a. (3), ethylbenzene is commercially produced by distilling the mixed xylene stream obtained by catalytically reforming the naphtha stream of crude petroleum. Only a small percentage of the total catalytic reformate output is used to isolate a mixed xylene product; most of it is blended into gasoline. In 1974, approximately 47,000 to 50,000 million pounds of mixed xylene were produced in catalytic reformate, but only 5,791 million pounds were isolated as a product (Carlson, 1975). Approximately 20% of mixed xylene is ethylbenzene.

The large amounts of catalytically reformed mixed xylenes blended into gasoline is reflected in the detectable quantity of ethylbenzene found in gasoline. Approximately 1.92% (by volume) of regular grade gasoline is ethylbenzene and 3.12% (by volume) of premium grade gasoline is ethylbenzene (Stavinoha and Newman, 1972). Ethylbenzene also exists naturally in crude petroleum at a concentration of 0.094% by weight (Martin and Winters, 1963).

Pyrolysis gasoline is obtained when paraffins, condensates, naphtha, and gas oil are cracked with intention of producing ethylene. Approximately 50 to 70 million pounds of pyrolysis gasoline are obtained for every 100 million pounds of ethylene produced (Carlson, 1975). The mixed xylenes comprise 10 to 12% by weight of this pyrolysis gasoline (Carlson, 1975) while

4 to 6 million pounds of styrene are produced per 100 million pounds of ethylene (Soder, 1977). Toray Industries of Japan is commercially developing a process to obtain the styrene portion of pyrolysis gasoline (Soder, 1977).

When styrene monomer is used to produce polymers and resins, a small percentage of styrene monomer will remain as a contaminant in the polymerized product. Approximately 0.10% styrene monomer and 0.06% ethylbenzene are present in a final polystyrene product (see Section II. B. 1. b. (1)). In 1976, about 4,200 million pounds of styrene copolymers were produced (Soder, 1977).

b. α-Methylstyrene and Divinylbenzene

If we assume that about 0.10% α-methylstyrene and divinylbenzene monomer remain as contaminants in their polymer products, then less than 100,000 pounds per year of each of the chemicals, contaminates their respective products.

B. Use Aspects

1. Consumption and Use Data

a. Ethylbenzene

Ethylbenzene consumption can be broken down as follows (SRC estimates; Paul and Soder, 1977):

| | |
|---|---|
| Production of Styrene | 97.5-98.5% |
| Exports | 1.5-2.5% |
| Solvents | <1% |
| | 100% |

Styrene production is described in detail in Section II. A. 3. b., and will not be discussed here. Approximately 2.5% of the domestic ethylbenzene production was exported in 1976 (U.S. Bureau of the Census, 1976);

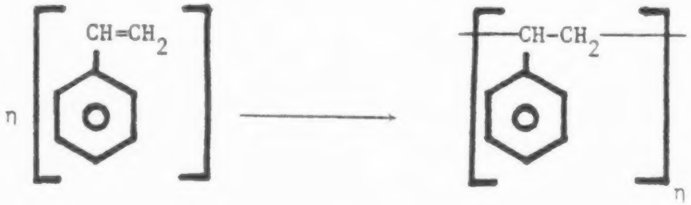
however, ethylbenzene exports may decline slightly in future years as production facilities come on-stream in foreign countries (Paul and Soder, 1977). Solvent use of ethylbenzene has been declining in recent years; it is used as a general purpose solvent, usually in combination with other solvents, in industrial plants.

b. Styrene

Table 15 lists the styrene consumption by end-use in 1975 and the estimates which are projected for 1980. The general recession in 1975 caused styrene consumption to decline almost 24% from the 1974 level; however, the percentage breakdown given in Table 15 is still quite accurate. Table 16 gives the estimated consumption of styrene by consumer and industrial product end-use markets in 1974; here, the emphasis is given to the final end-use product. A general description of the various uses listed in Table 15 follows.

(1) Polystyrene

About 55% of all styrene consumed in the U.S. is used to make polystyrenes. The polymerization of styrene is a chain reaction which proceeds readily by all known polymerization techniques; the reaction can be shown schematically as (Griffin and Glass, 1974):



The polymer can be characterized by the distribution of η values. The polymerization reaction is activated by heat alone; however, peroxides are used commercially to accelerate the process (Haddad, 1976).

Table 15. Styrene Consumption by End-Use in 1975 and Estimates for 1980 (adapted from Soder, 1977; Chem. & Eng. News, 1977)

| | 1975 | | 1980 | |
|---|---|---|---|---|
| | Styrene Consumption (Millions of Pounds) | Percent | Styrene Consumption (Millions of Pounds) | Percent |
| Straight Polystyrene | 1,383 | 28.5 | 4,100 | 55 |
| Impact Polystyrene | 1,278 | 26.5 | | |
| ABS Resins | 347 | 7 | 750 | 10 |
| SAN Resins | 61 | 1.5 | 125 | 1.5 |
| Styrene-Butadiene Copolymer Latexes | 287 | 6 | 410 | 5.5 |
| Other Copolymers over 50% Styrene | 81 | 1.5 | 142 | 2 |
| SBR Elastomers | 459 | 9.5 | 625 | 8.5 |
| Unsaturated Polyester Resins | 312 | 6.5 | 520 | 7 |
| Misc. Polymers less than 50% Styrene | 50 | 1 | 100 | 1.5 |
| Exports | 574 | 12 | 685 | 9 |
| Other | < 5 | < 1 | < 5 | < 1 |
| TOTAL | 4,837 | 100% | 7,462 | 100% |

Table 16. Estimated Consumption of Styrene by Consumer and Industrial Product End-Use Markets - 1974 (Soder, 1977)

| | Estimated Consumption (Millions of Pounds) | | Percent of Total |
|---|---|---|---|
| Packaging | | 1,100 | 22 |
| Construction-Related Markets | | 789-797 | 16 |
| Construction | 261-265 | | |
| Pipe | 253-255 | | |
| Industrial rubber products | 177 | | |
| Lighting fixtures and signs | 50 | | |
| Paint | 22 | | |
| Corrosion-resistant products | 26-28 | | |
| Electrical, Appliance, TV, Communication, and Office Machines-Related Markets | | 620-624 | 12 |
| Appliance and TV | 339 | | |
| Electrical and other | 281-285 | | |
| Household (except appliances) | | 582-589 | 12 |
| Housewares and furnishings | 285 | | |
| Carpeting and flooring | 151 | | |
| Furniture | 116-120 | | |
| Synthetic marble | 30-33 | | |
| Transportation-Related Markets | | 477-484 | 10 |
| Tires | 315 | | |
| Auto, truck, bus parts | 139-142 | | |
| Auto putty | 15-19 | | |
| Miscellaneous transportation | 8 | | |
| Recreation-Related Markets | | 408-414 | 8 |
| Toys, sporting goods, miscellaneous recreational articles | 322-324 | | |
| Marine (pleasure boats) | 52-56 | | |
| Recreational vehicles | 34 | | |
| Disposable Serviceware | | 230 | 4 |

Table 16. Estimated Consumption of Styrene by Consumer and Industrial Product End-Use Markets - 1974 (Soder, 1977) (Cont'd)

| | | | | |
|---|---|---|---|---|
| Miscellaneous | | | 536-546 | 11 |
| Industrial products | | 233-238 | | |
| Paper coatings & additives | 128 | | | |
| Ion-exchange resins | 45-50 | | | |
| Medical/dental/lab equipment | 50 | | | |
| Impact modifiers | 10 | | | |
| Consumer products | | 214-216 | | |
| Novelties & other uses | 95 | | | |
| Writing utensils | 54 | | | |
| Personal care items | 50 | | | |
| Luggage & cases | 11 | | | |
| Floor polishes | 4-6 | | | |
| Other | | 89-92 | | |
| Exports | | | 241-243 | 5 |
| TOTAL | | | 4,933-5,027 | 100% |

Two general classes of polystyrenes are produced: (1) "straight" or homopolymer polystyrenes and (2) impact or "rubber modified" polystyrenes. Straight polystyrene is a water-white, transparent plastic with an unlimited colorability range which is widely used in packaging, toys, housewares, and appliances. It can easily be molded or extruded into practically any shape or form. Expanded foams of polystyrene have excellent heat-insulating and flotation properties and find application in construction and refrigeration, as well as numerous uses in packaging and drinking cups. Impact polystyrenes contain 3 to 10% elastomer (e.g., polybutadiene), which decreases the brittleness of the resin and considerably expands the number of applications. It is not transparent like the homopolymer, but it is much more durable. Packaging applications account for about one-third the use of all polystyrenes produced (Soder, 1977).

As might be expected, a small amount of styrene monomer remains in the final polystyrene product as a contaminant. Table 17 below gives an analysis of styrene monomer and ethylbenzene content in various polystyrene products chosen at random.

Table 17. Analysis of Various Grades of Polystyrene (Crompton and Myers, 1968).

| | Weight per cent | | | | |
|---|---|---|---|---|---|
| Component | Crystal grade | Expandable grade | Self extinguishing grade | High impact grade | Foodstuff packaging grade |
| Styrene | 0.033 | 0.32 | 0.080 | 0.18 | 0.04 |
| Ethylbenzene | 0.066 | 0.081 | 0.047 | 0.086 | 0.06 |

Approximately 3,200 million pounds of polystyrenes were produced in 1976 (Soder, 1977). If we assume that 0.10%, on average, styrene monomer remains in the polystyrene as contaminant, then 3.2 million pounds of styrene contaminated polystyrene products in 1976. Similarly, assuming ethylbenzene at 0.06%, on average, yields 1.92 million pounds of contamination.

### (2) ABS Resins

ABS (acrylonitrile-butadiene-styrene) resins are produced by the co-polymerization of acrylonitrile and styrene monomers in the presence of butadiene rubber. The resultant styrene-acrylonitrile (SAN) co-polymers are grafted onto the rubber particles to yield hard, tough, chemically resistant plastics (Morneau, 1976). ABS resins typically contain 50 to 60% styrene (Soder, 1977); however, after polymerization, the final product will contain only a small percentage of styrene monomer.

Uses for ABS resins are the following (Chem. Prof., 1977a): pipes and fittings (drain, waste, and vent), 29%; automotive, 18%; large appliances, 14%; small appliances, 5%; recreational vehicles, 8%; business machines and telephones, 5.2%; furniture, luggage, and packaging, 6.1%; exports, 3.2%; miscellaneous, 11.5%.

### (3) SAN Resins

SAN (styrene-acrylonitrile) resins are transparent, rigid thermoplastics with properties slightly different and somewhat intermediate to those of polystyrene and ABS. They are produced by the copolymerization of styrene, 60 to 80%, and acrylonitrile, 20 to 40% (Soder, 1977). Application of SAN resins include automobile instrument panel windows and lenses, clear houseware items, and appliances.

### (4) Styrene-Butadiene Copolymer Latexes

Styrene-butadiene copolymer, which contains upward of 50% styrene (as compared to synthetic styrene-butadiene rubber which is made from the same ingredients but is only 20% styrene), is a latex material used as an emulsion in the manufacture of paint and surface coatings for cloth and paper. The primary uses are carpetback coatings and paper coatings.

### (5) Other Copolymers Over 50% Styrene

Styrene-divinylbenzene resins, the most important copolymer of this classification, are formed by crosslinking polystyrene beads with divinylbenzene and are the most common matrix base for ion exchange resins. Typically, styrene-divinylbenzene ion-exchange resin is produced from 92% styrene and 8% divinylbenzene. The major uses of ion-exchange resins are water-treatment (softening and deionization) and chemical processing. In 1975, 64 to 69 million pounds of styrene were consumed in production of styrene-divinylbenzene resins (Soder, 1977).

Less than 5 million pounds of styrene were consumed in 1975 in the production of styrene-maleic anhydride copolymers. They are used in floor polishes, textile and paper sizing, rug shampoos, and latex paint. The styrene/maleic anhydride mole ratio is typically 1:1 to 3:1 (Soder, 1977).

K-Resin® is a transparent styrene-butadiene copolymer film, sheet, and injection molding resin that is believed to contain 75% styrene and 25% butadiene. It has been made since 1973 by Phillips Petroleum; plant capacity is currently 18 million pounds per year (Soder, 1977).

Methyl methacrylate-butadiene-styrene (MBS) resins are used as impact modifiers for rigid PVC; commercial development was only begun in

1974. Industry capacity for MBS resins is at least 35 million pounds per year (Soder, 1977).

### (6) SBR Elastomers

Styrene-butadiene elastomers (SBR) account for the bulk of all elastomers used in passenger cars and lightweight truck tires. The newer SBR polymers contain about 21% styrene (Soder, 1977). When more than 50% styrene is used in combination with butadiene, the resulting polymers generally are more like plastics than rubbers. SBR elastomers find the following applications (Chem. Prof., 1977b): tires and tire products, 68%; molded and extruded goods, 13%; sponge, 4%; footwear, 3%; miscellaneous, 12%.

Vinyl pyridine-styrene-butadiene latexes, which are included in SBR production data, are primarily used in tire cord adhesives.

### (7) Unsaturated Polyester Resins

Unsaturated polyester resins are thermosetting resins used primarily in fiberglass reinforced plastics (FRP) for marine, construction, and transportation applications; other products include synthetic marble and a variety of consumer goods (Soder, 1977).

The resins are formed by polycondensation of dicarboxylic acids or anhydrides (such as maleic anhydride, phthalic anhydride, and isophthalic acid) with glycols (such as propylene glycol and ethylene glycol); the polycondensate is then dissolved in styrene, which, when catalytically activated, crosslinks through the unsaturated bonds of the dicarboxylic acids or anhydrides. Actual compositions of polyester resins vary widely, but typical styrene content is in the range of 30 to 50 weight percent of the final resin product (exclusive of reinforcement) (Soder, 1977).

(8) Miscellaneous Polymers Less Than 50% Styrene

Acrylic ester-styrene copolymers used in acrylic thermosetting solvent-based surface coatings typically contain 0 to 50 weight percent styrene in combination with ethyl acrylate and acrylamide. These coatings are used in industrial applications, primarily in topcoats for automobiles, trucks, and buses. Styrene consumption for these copolymers is estimated at 19 to 22 million pounds annually (Soder, 1977).

Acrylic and methacrylic ester-styrene copolymers containing 1 to 20% styrene are used in floor polish formulations. Maximum styrene consumption for these products is estimated at 4 to 6 million pounds per year (Soder, 1977).

Styrene-polydiene block copolymer thermoplastic elastomers, that contain 70% butadiene (or isoprene) and 30% styrene, are used in footwear, adhesives, and miscellaneous molded and extruded goods. Styrene consumption for this use may have been 9 to 11 million pounds in 1975.

Styrenated alkyds for use in alkyd surface coatings are generally formed by adding styrene modifier to a preformed alkyd resin; up to 40% styrene can be added, but 10 to 25% is more common. Styrene consumption for this production is probably a maximum of 7 to 8 million pounds annually.

(9) Other

Styrenated phenols are used as rubber antioxidants; total production of styrenated phenols was 2.1 million pounds in 1974 and 0.5 million pounds in 1975 (USITC, Annual a). About 1 to 2 million pounds per year of styrene oxide are produced; styrene oxide can be used as a reactive diluent in epoxy resin manufacture and in specialty polyol manufacture (Soder, 1977).

Styrene oxide is produced by Union Carbide at Taft, Louisiana (SRI, 1977). Small amounts of styrene are also used in the production of styrenated oils (Soder, 1977).

### c. α-Methylstyrene

Virtually all of the α-methylstyrene that is commercially recovered is used in the formulation of specialty polymers and resins. It is widely used in modified polyester and alkyd resin formulations where its distinctive properties, such as light color, are valuable. Copolymers of α-methylstyrene and methylmethacrylate have high heat-distortion resistance properties and have been approved for use in food applications. Low-molecular-weight α-methylstyrene polymers are viscous liquids that are used as plasticizers in paints, waxes, adhesives, and plastics. The main use in specialty resins appears to be in ABS resins used in automobiles (Chem. Prof., 1974a; Coulter *et al.*, 1969).

More than 20% of the domestic production has been exported in recent years; expansion of domestic production was apparently done to serve the increased demand in the export market (Chem. Prof., 1974a).

### d. Divinylbenzene

Most of the divinylbenzene production is used in the manufacture of ion-exchange resins. Styrene-divinylbenzene resins formed by cross-linking polystyrene beads with divinylbenzene are the most common matrix base for ion-exchange resins. A typical styrene-divinylbenzene resin contains 92% styrene and 8% divinylbenzene. Other ion-exchange matrixes made from divinylbenzene include methyl acrylate-divinylbenzene copolymers (Soder, 1977). The major uses of these ion-exchange resins are water-treatment (softening and deionization) and chemical processing (such as, sugar purification, pharmaceutical manufacture, and uranium processing). Divinylbenzene also finds applications in styrene-butadiene rubber; the swelling, shrinkage, and extrusion properties of the product are improved by adding small amounts of the monomer to the formulation (Coulter et al., 1969).

### 2. Use Sites

Table 18 lists the use sites for styrene and divinylbenzene monomers. Ethylbenzene use sites are basically the styrene production sites. α-Methylstyrene is mainly used in ABS-type resins, so the ABS production sites listed in Table 18 may be a good indication of the use sites for α-methylstyrene. Amoco Chemicals (Texas City, Texas) produces a linear α-methylstyrene polymer (SRI, 1977).

### 3. Application of Products Containing Contaminants

Most of the polymer products made from the subject chemicals will contain a small percentage of the monomer as a contaminant in the final product. The application of these polymer products has previously been described in Section II. B. 1. Corporate tradenames for various polymer products are given in Table 19.

#### a. Ethylbenzene

The major product which contains ethylbenzene as a contaminant is mixed xylenes (see Section II. A. 5). Most of these xylenes are never isolated from the refinery streams of which they are components, but are simply blended into gasoline because of the high octane rating of mixed xylenes. The mixed xylene which is isolated has several applications. Most importantly, it is used as a source of the individual isomers of xylene and as a source for commercial ethylbenzene (see Section II. B. 3. a. (3)). In 1974, 150 million

Table 18. Use Sites for Styrene and Divinylbenzene Monomer
(SRI, 1977; Soder, 1977; Frey, 1976; Chem. Prof., 1977a,b, 1974b)

| | | Polystyrene | ABS & SAN Resins | Styrene-Butadiene Copolymers | SBR Latexes & Elastomers | Styrene-Divinylbenzene Copolymers | Styrene-Maleic Anhydride | MBS Resins | Polybutadiene-Styrene-vinyl-pyridine Latexes Unsaturated | Polyester Resins |
|---|---|---|---|---|---|---|---|---|---|---|
| A & E Plastik Pak Co. | City of Industry, Calif. | X | | | | | | | | |
| Abtec | Louisville, Ky. | | X | | | | | | | |
| Alpha Chem. Corp. | Colliersville, Tenn. | | | | | | | | | X |
| | Kathleen, Fla. | | | | | | | | | X |
| | Riverside, Calif. | | | | | | | | | X |
| American Cyanamid | Azuza, Calif. | | | | | | | | | X |
| | Wallingford, Conn. | | | | | | | | | X |
| American Synthetic Rubber | Louisville, Ky. | | | X | X | | | | | |
| Amoco Chem. Co. | Joliet, Ill. | X | | | | | | | | |
| | Medina, Ohio | X | | | | | | | | |
| | Torrance, Calif. | X | | | | | | | | |
| | Williow Springs, Ill. | X | | | | | | | | |
| ARCO Chem. | Channelview, Tex. | | | | | | X | | | |
| ARCO/Polymers Inc. | Beaver Valley, Pa. | | | X | X | | | | | |
| Ashland Oil Co. | Baytown, Tex. | | | | X | | | | | |
| | Calumet City, Ill. | | | | | | | | | X |
| | Los Angeles, Calif. | | | | | | | | | X |
| | Newark, N.J. | | | | | | | | | X |
| | Pensacola, Fla. | | | | | | | | | X |
| | Valley Park, Mo. | | | | | | | | | X |
| BASF Wyandotte | Jamesburg, N.J. | X | | | | | | | | |
| Beatric Food Co. | Wilmington, Mass. | X | | | | | | | | |

Table 18. Use Sites for Styrene and Divinylbenzene Monomer (Cont'd)
(SRI, 1977; Soder, 1977; Frey, 1976; Chem. Prof., 1977a,b, 1974b)

| | | Polystyrene | ABS & SAN Resins | Styrene-Butadiene Copolymers | SBR Latexes & Elastomers | Styrene-Divinylbenzene Copolymers | Styrene-Maleic Anhydride | MBS Resins | Polybutadiene-Styrene-vinyl-pyridine Latexes Unsaturated | Polyester Resins |
|---|---|---|---|---|---|---|---|---|---|---|
| Borden Inc. | Bainbridge, N.Y. | X | | | | | | | | |
| | Compton, Calif. | X | | | | | | | | |
| | Demopolis, Ala. | X | | | | | | | | |
| | Illiopolis, Ill. | X | | X | X | | | | | |
| | Leominster, Mass. | X | | | X | | | | | |
| Borg-Warner | Ottawa, Ill. | | X | | | | | | | |
| | Washington, W.Va. | | X | | | | | X | | |
| Cargill, Inc. | Carpentersville, Ill. | | | | | | | | | X |
| | Lynwood, Calif. | | | | | | | | | X |
| Celanese Corp. | Charlotte, N.C. | | | | X | | | | | |
| Cook Paint & Varnish Co. | Detroit, Mich. | | | | | | | | | X |
| | Milpitas, Calif. | | | | | | | | | X |
| | North Kansas City, Mo. | | | | | | | | | X |
| Copolymer Rubber & Chem. | Baton Rouge, La. | | | | X | | | | | |
| Cosden Oil & Chem. | Big Spring, Tex. | X | | | | | | | | |
| | Calumet City, Ill. | X | | | | | | | | |
| Deering-Milliken | Inman, S.C. | | | | | | | | X | |
| Dewey and Almy Chem. | Owensburg, Ky. | | | X | X | | | | | |
| | South Acton, Mass. | | | X | X | | | | | |
| Diamond Shamrock | Deer Park, Tenn. | | | | | X | | | | |
| | Oxnard, Calif. | | | | | | | | | X |

Table 18. Use Sites for Styrene and Divinylbenzene Monomer (Cont'd) (SRI, 1977; Soder, 1977; Frey, 1976; Chem. Prof., 1977a,b, 1974b)

| | | Polystyrene | ABS & SAN Resins | Styrene-Butadiene Copolymers | SBR Latexes & Elastomers | Styrene-Divinylbenzene Copolymers | Styrene-Maleic Anhydride | MBS Resins | Polybutadiene-Styrene-vinyl-pyridine Latexes Unsaturated | Polyester Resins |
|---|---|---|---|---|---|---|---|---|---|---|
| Dow Chem. | Allyn's Point, Conn.* | X | | | | | | | | |
| | Dalton, Ga. | | | | X | | | | | |
| | Freeport, Tex. | | | X | | | | | | |
| | Gales Ferry, Conn.* | X | X | | X | | | | | |
| | Ironton, Oh. | X | | | | | | | | |
| | Magnolia, Ark. | X | | | | | | | | |
| | Midland, Mich. | X | X | X | X | X | | | | |
| | Pevely, Mo. | X | X | | | | | | | |
| | Pittsburg, Calif. | | | X | X | | | | | |
| | Torrance, Calif. | X | X | | | | | | | |
| Firestone Tire & Rubber | Akron, Oh. | | | X | X | | | | | |
| | Pottstown, Pa. | | | | X | | | | | |
| | Lake Charles, La. | | | | X | | | | | |
| Foster Grant | Chesapeak, Va. | X | | | | | | | | |
| | Leominster, Mass. | X | X | | | | | | | |
| | Peru, Ill. | X | | | | | | | | |
| Freeman Chem. Corp. | Chatham, Va. | | | | | | | | | X |
| | Saukville, Wisc. | | | | | | | | | X |
| GAF Corp. | Chattanooga, Tenn. | | | X | X | | | | | |
| General Tire & Rubber | Mogadore, Oh. | | | X | | | | | X | |
| | Odessa, Tex. | | | X | | | | | | |
| B.F. Goodrich | Louisville, Ky. | | X | X | | | | | | |
| | Port Neches, Tex. | | | | X | | | | | |

*same site

Table 18. Use Sites for Styrene and Divinylbenzene Monomer (Cont'd)
(SRI, 1977; Soder, 1977; Frey, 1976; Chem. Prof., 1977a,b, 1974b)

| | | Polystyrene | ABS & SAN Resins | Styrene-Butadiene Copolymers | SBR Latexes & Elastomers | Styrene-Divinylbenzene Copolymers | Styrene-Maleic Anhydride | MBS Resins | Polybutadiene-Styrene-vinyl-pyridine Latexes Unsaturated | Polyester Resins |
|---|---|---|---|---|---|---|---|---|---|---|
| Goodyear Tire & Rubber | Akron, Oh. | | | | X | | | | | |
| | Houston, Tex. | | | | X | | | | | |
| Hammond Plastics | Worcester, Mass. | X | X | | | | | | | |
| | Oxford, Mass. | X | X | | | | | | | |
| Hatco Polyester | Bartow, Fla. | | | | | | | | | X |
| | Colton, Calif. | | | | | | | | | X |
| | Jacksonville, Ark. | | | | | | | | | X |
| | Linden, N.J. | | | | | | | | | X |
| | Swanton, Ohio | | | | | | | | | X |
| Hercules Inc. | Clairton, Pa. | X | | | | | | | | |
| Hooker Chem. Corp. | North Tonawanda, N.Y. | | | | | | | | | X |
| ICI United States | Wilmington, Del. | | | | | | | | | X |
| Interplastic Corp. | Jackson, Miss. | | | | | | | | | X |
| | Minneapolis, Minn. | | | | | | | | | X |
| | Pryor, Okla. | | | | | | | | | X |
| Ionac Chem. | Birmingham, N.J. | | | | | X | | | | |
| Koppers Co. | Bridgeville, Pa. | | | | | | | | | X |
| | Richmond, Calif. | | | | | | | | | X |
| Monsanto | Addyston, Oh. | X | X | | | | X | | | |
| | Decatur, Ala. | X | | | | | | | | |
| | Long Beach, Calif. | X | | | | | | | | |
| | Springfield, Mass. | X | | | | | | | | |

Table 18. Use Sites for Styrene and Divinylbenzene Monomer (Cont'd)
(SRI, 1977; Soder, 1977; Frey, 1976; Chem. Prof., 1977a,b, 1974b)

| | | Polystyrene | ABS & SAN Resins | Styrene-Butadiene Copolymers | SBR Latexes & Elastomers | Styrene-Divinylbenzene Copolymers | Styrene-Maleic Anhydride | MBS Resins | Polybutadiene-Styrene-vinyl-pyridine Latexes Unsaturated | Polyester Resins |
|---|---|---|---|---|---|---|---|---|---|---|
| Monsanto (Cont'd) | Muscatine, Iowa | | X | | | | | | | |
| | Everett, Mass. | | | | | | X | | | |
| Morton-Norwich Products | Ringwood, Ill. | X | | | | | | | | |
| Owens-Corning Fiberglas | Anderson, S.C. | | | | | | | | | X |
| | Valparaiso, Ind. | | | | | | | | | X |
| Phillips Petroleum | Borger, Tex. | | | X | X | | | | | |
| Polysar Plastics | Forest City, N.C. | X | | | | | | | | |
| PPG Industries | Circleville, Oh. | | | | | | | | | X |
| | Houston, Tex. | | | | | | | | | X |
| | Springdale, Pa. | | | | | | | | | X |
| | Torrance, Calif. | | | | | | | | | X |
| Pressure Chem. Co. | Pittsburg, Pa. | X | | | | | | | | |
| Purex Chem. Co. | Bristol, Pa. | X | | | | | | | | |
| | Carson, Calif. | X | | | | | | | | |
| Reichhold Chem. | Azuza, Calif. | X | | | | | | | | X |
| | Detroit, Mich. | X | | | | | | | | X |
| | Elizabeth, N.J. | X | | | | | | | | X |
| | Grand Junction, Tenn. | | | | | | | | | X |
| | Houston, Tex. | | | | | | | | | X |
| | Jacksonville, Fla. | | | | | | | | | X |
| | Morris, Ill. | | | | | | | | | X |
| | South San Francisco, Cal. | | | | | | | | | X |
| | Tacoma, Wash. | | | | | | | | | X |

Table 18. Use Sites for Styrene and Divinylbenzene Monomer (Cont'd)
(SRI, 1977; Soder, 1977; Frey, 1976; Chem. Prof., 1977a,b, 1974b)

| | | Polystyrene | ABS & SAN Resins | Styrene-Butadiene Copolymers | SBR Latexes & Elastomers | Styrene-Divinylbenzene Copolymers | Styrene-Maleic Anhydride | MBS Resins | Polybutadiene-Styrene-vinyl-pyridine Latexes Unsaturated | Polyester Resins |
|---|---|---|---|---|---|---|---|---|---|---|
| The Richardson Co. | Channelview, Tex. | X | | | | | | | | |
| | Madison, Conn. | X | | | | | | | | |
| | West Haven, Conn. | X | | | | | | | | |
| Rexene (Dart Industries) | Holyoke, Mass. | X | | | | | | | | |
| | Joliet, Ill. | X | X | | | | | | | |
| | Ludlow, Mass. | X | | | | | | | | |
| | Santa Ana, Calif. | X | | | | | | | | |
| Rockwell International | Astabula, Oh. | | | | | | | | | X |
| Rohm & Haas Co. | Philadelphia, Pa. | | | | | X | | X | | |
| | Bridgeburg, Pa. | | | | | | | | | X |
| | Knoxville, Tenn. | | | | | | | | | X |
| SCM Corp. | Chicago, Ill. | | | | | | | | | X |
| | Cleveland, Oh. | | | | | | | | | X |
| | Huron, Oh. | | | | | | | | | X |
| | Reading, Pa. | | | | | | | | | X |
| | San Francisco, Calif. | | | | | | | | | X |
| Shell Chem. | Belpre, Oh. | X | | | | | | | | |
| | Leominster, Mass. | X | | | | | | | | |
| A.E. Staley Mfg. Co. | Kearney, N.J. | X | | | | | | | | |
| | Lemont, Ill. | X | | | | | | | | |
| Stepan Chem. Co. | Anahiem, Calif. | | | | | | | | | X |
| Solar Chem. Corp. | Chattanooga, Tenn. | | | | X | | | | | |

Table 18. Use Sites for Styrene and Divinylbenzene Monomer (Cont'd)
(SRI, 1977; Soder, 1977; Frey, 1976; Chem. Prof., 1977a,b, 1974b)

| | | Polystyrene | ABS & SAN Resins | Styrene-Butadiene Copolymers | SBR Latexes & Elastomers | Styrene-Divinylbenzene Copolymers | Styrene-Maleic Anhydride | MBS Resins | Polybutadiene-Styrene-vinyl-pyridine Latexes Unsaturated | Polyester Resins |
|---|---|---|---|---|---|---|---|---|---|---|
| Southwest Latex | Bayport, Tex. | | | X | X | | | | | |
| Sterling Plastics | Orange, Calif. | X | | | | | | | | |
| | Windsor, N.J. | X | | | | | | | | |
| Sybron Corp. | Birmingham, N.J. | X | | | | | | | | |
| | Haledon, N.J. | X | | | | | | | | |
| Texas Chem. & Plastics | Longbeach, Calif. | X | | | | | | | | |
| Texas - U.S. Chem. | Port Neches, Tex. | | | | X | | | | | |
| Tylac Chem. | Cheswold, Del. | | | X | X | | | | | |
| | Kensington, Ga. | | | X | X | | | | | |
| Union Carbide | Bound Brook, N.J. | X | X | | | | | | | |
| | Marietta, Oh. | X | | | | | | | | |
| Union Oil Co. | Charlotte, N.C. | | | X | X | | | | | |
| | LaMirada, Calif. | | | X | X | | | | | |
| U.S. Industries Inc. | Copley, Oh. | X | | | | | | | | |
| U.S. Steel Corp. | Haverhill, Oh. | X | | | | | | | | |
| Uniroyal | Baton Rouge, La. | | X | | | | | | | X |
| | Scotts Bluff, La. | | X | X | X | | | | | |
| Vistron Corp. | Covington, Ky. | | | | | | | | | X |
| | Hawthorne, Calif. | | | | | | | | | X |
| Whittaker Corp. | Lenoir, N.C. | | | | | | | | | X |
| | Minneapolis, Minn. | | | | | | | | | X |

## Table 19. Tradenames for Various Polymer Products

---

### Polystyrene

Styron (Dow)
Styrofoam (Dow)
Lustrex (Monsanto)
Tuf-Flex (Foster-Grant)
Styropar (BASF Wyandotte)
Helman (U.S. Industries)
Rexene 400 FR1 (Rexene)
Shell 351 (Shell Chem.)
Trycite (Dow)
Pelaspan-Pac (Dox)

### ABS Resins

Dow ABS (Dow)
Lustran (Monsanto)
Terluran (ARCO/Polymers)
Fosta-plus (Foster Grant)
Abson (B.F. Goodrich)
Cycolac (Borg-Warner)
Rexene 500 FR1 (Rexene)
Kralastic (Uniroyal)
Royalite (Uniroyal)

### SAN Resins

Tyril (Dow)
Lustran SAN (Monsanto)
Luran (ARCO/Polymers)
Acrylafil (Rexene)

### Styrene-Butadiene Copolymers

Dow Latex Series 200-600 (Dow)
K-Resin (Phillips Petroleum)
Amsyn$^{\text{TM}}$ (American Synthetic Rubber)

### SBR (Polybutadiene-styrene & latex)

Flosbrene (American Synthetic Rubber)
Copo (Copolymer Rubber & Chem.)
FR-S (Firestone Tire)
Ameripal SBR (B.F. Goodrich)
Plioflex (Goodyear)
Philprene (Phillips Petroleum)
Synpol (Texas-U.S. Chem.)

### Styrene-Divinylbenzene Resins

Duolite (Diamond Shamrock)
Dowex (Dow)
Amerlite (Rohm & Haas)
Ionac (Ionac Chem.)

### Polybutadiene-Styrene-Vinylpyridine Latex

Gen-Tac (General Tire)
Chemivic (Goodyear)
Vithane (Goodyear)
Pyratex (Uniroyal)

gallons of mixed xylenes (which has a content of 20% ethylbenzene) were used as industrial solvents (Carlson, 1975). As solvents, mixed xylenes are not used alone but can be classified as diluents because they are blended with other solvents. The paint industry consumed nearly half of the solvent mixed xylenes in 1974 (Carlson, 1975). Mixed xylenes have been used alone in agricultural sprays where they serve as the carrier for the pesticides being applied. The use of mixed xylenes as an agricultural solvent is expected to decline as recent regulations require such solvents to have a higher flash point than xylene (Carlson, 1975). Isolated mixed xylenes are also blended into gasoline.

#### b. Styrene

As explained in Section II. A. 5. a., styrene is a contaminant by-product in pyrolysis gasoline produced when paraffins, condensates, naphtha, and gas oil are cracked with the intention of producing ethylene. This pyrolysis gasoline is blended into gasoline and fuel oils, depending upon composition.

### 4. Projected or Proposed Uses

The patent literature contains numerous patents describing the use of styrene, α-methylstyrene, and divinylbenzene in polymer products. Which particular polymers may become commercially important in the future cannot be projected at this time. However, because of the polymerization characteristics of these chemicals, especially styrene and divinylbenzene, it is unlikely that any large scale application will be developed which does not involve polymerization.

### 5. Alternatives to Use

Because most of the ethylbenzene which is commercially produced is used to make styrene, an alternative to ethylbenzene use would require that styrene be made from some other chemical process. Such a process has been proposed. A recent patent (U.S. 3,965,206) to Monsanto proposes production of styrene from toluene and ethylene via stilbene. Basic process evaluations suggest the economics for this process are quite promising compared to ethylbenzene routes (Soder, 1977).

Virtually all of the styrene, α-methylstyrene, and divinylbenzene produced is used to make polymer products such as plastics, synthetic rubbers, and latexes. It may be theoretically possible to state that most uses of these polymer products could be substituted by an alternative product. For example, from Table 16, it can be seen that about 20% of the annual styrene consumption is used in packaging products; alternatives, such as paper products, could be substituted for this use. Additionally, all of the styrene polymers used to make plastics for appliances, housewares, toys, and automobiles could be substituted by glasses and metals. However, styrene products are used for reasons of economics, safety, and convenience and, therefore, may be difficult to replace.

## C. Entry Into the Environment

### 1. Points of Entry

#### a. Production

Sources of emissions from styrene production have been examined by Pervier et al. (1974). Styrene emissions can result from vents on distillation columns and other process equipment, storage tank losses, miscellaneous leaks and spills, process wastewaters, and solid process wastes. Similar points of release can probably be applied to production of ethylbenzene, α-methylstyrene, and divinylbenzene.

The severity of losses from production varies from plant to plant; however, according to Pervier et al. (1974), emissions from styrene production are low in comparison to other petrochemical industries which have been surveyed. Fuller et al. (1976) have estimated the production losses from ethylbenzene to be 1%. An EPA funded study by Hydroscience (Contract 68-02-2577) of ethylbenzene plants has suggested a much lower figure. The accuracy of these estimates is not known.

### b. Use

Styrene, α-methylstyrene, and divinylbenzene are basically used in polymer production. Pervier et al. (1974) indicate that styrene can be emitted from polymerization processes from dryer vents, from some wastewater and solid wastes, and from some fugitive emissions from reactors. Other losses could result from various leaks and spills. Fjeldstad et al. (1979) and Pfäffli et al. (1979) have both shown that considerable amounts of styrene (50-150 ppm) and styrene oxide (0.03 - 0.2 ppm) can be detected in polyester fabrication plants and therefore losses to the environment also seem likely. The styrene oxide is thought to be produced by the peroxide curing agent.

Relatively small amounts of ethylbenzene are used for solvent purposes as compared to amounts used to manufacture styrene. However, in these uses, substantial quantities of ethylbenzene may be allowed to vaporize from exposure to air. The nature of the use will probably determine the potential for emission.

### c. By-Product or Contaminant

As mentioned in Section II. A. 5, ethylbenzene is produced as a by-product in catalytic reformate and pyrolysis gasoline. Styrene is also a by-product in pyrolysis gasoline. The processes which produce catalytic reformate and pyrolysis gasoline are general petrochemical operations which have the potential to make emissions from distillation column or process equipment vents, and from leaks, spills, etc. These process emission sources are probably quite small, however, as compared to emission potential from use of the catalytic reformate chemicals. Large quantities of these chemicals are blended into gasolines. Stavinoha and Newman (1972) and Sanders and Maynard (1968) have determined amounts of ethylbenzene in motor gasolines in volume and weight amounts up to 3%. It is possible that significant amounts of ethylbenzene are emitted from gasoline when vapors escape from filling an automobile with gasoline at a service station.

### d. Miscellaneous Disposal

Grossman (1970) has detailed an example of unique styrene release to the environment in Connecticut. During construction of a residential development in Gales Ferry, Connecticut, waste styrene had been used to burn brush in clearing land because of the intense heat generated when styrene undergoes combustion. At least two leftover drums of styrene, partially filled, were buried beneath one to four feet of fill at two separate places at Gales Ferry. Within several years, the new residents at Gales Ferry noticed contamination of well water; it was identified as styrene. The buried drums of styrene were removed from the area but styrene contamination in the water persisted at a declining rate for two years. Grossman (1970) concluded that the styrene contamination from the buried drums was due to the unique geological make-up of the area.

### e. Monomer Migration from Polystyrene

As mentioned in Section II. B. 1. b, a small percentage of styrene monomer is present in finished polystyrene products. Davies (1974) has monitored styrene migration from polystyrene packaging materials into food. The rate of migration is apparently dependent upon monomer concentration, temperature, food type, and other parameters.

## 2. Emission and Effluent Control Methods

Pervier et al. (1974) briefly discuss the pollution and emission control methods used by the styrene manufacturing industry. Emissions from vents, such as distillation columns, are normally channelled through some kind of condensible vapor conservation system to recover valuable products for recycle or use. Some vent emissions can be burned as fuels for process operations. Solid process wastes, such as spent catalyst and filter aids, are usually disposed to sanitary landfills. About 500 pounds of catalyst are disposed of for every million pounds of styrene product. Spilled materials are normally disposed to landfills also.

Process wastewaters are normally sent to on-site treatment lagoons. Treatment varies from plant to plant, but usually includes neutralization and filtration. Varying degrees of process wastewaters, both treated and untreated, can be recycled. One petrochemical plant's five-day lagoon effluent was monitored to have a styrene concentration of 0.03 mg/liter (Webb et al., 1973).

It is judged that similar emission controls and methods are utilized by ethylbenzene, α-methylstyrene, and divinylbenzene manufacturers.

Users of styrene have had styrene detected in their wastewaters. A synthetic rubber plant's settling pond contained a styrene level of 0.003 mg/liter (Webb et al., 1973).

### 3. Production in the Environment

#### a. Motor Vehicle Exhausts

Table 20 lists the representative volume compositions of hydrocarbon components of vehicular emissions which Schofield (1974) obtained from General Motors Laboratories. It can be seen from Table 20 that ethylbenzene is present in vehicle exhausts as well as some styrene. The EPA estimated that in 1974, about 12.5 million tons of hydrocarbons were emitted by motor vehicles (Council on Environmental Quality, 1975). If it is assumed that the average volume composition of all vehicular emissions is 0.60% ethylbenzene, then it can be calculated that roughly 280 million pounds of ethylbenzene are emitted per year from motor vehicle exhausts. This is equivalent to about 4% of the total amount of ethylbenzene manufactured industrially each year. Similar but less quantitative estimates can be calculated for styrene (styrene value is combined with o-xylene value).

#### b. Combustion Systems

Styrene has been detected in hydrocarbon exhausts from spark-ignition engines utilizing specific fuel types (Fleming, 1970). Fleming (1970) identified styrene in exhausts from fuel compositions containing large quantities of m-xylene; Fleming (1970) additionally showed that exhaust compositions from spark-ignition engines are dependent upon aromatics in the fuel.

Styrene and methylstyrenes have also been identified in oxy-acetylene and oxy-ethylene flames (Crittenden and Long, 1976). It is possible, therefore, that styrene may be emitted from motor vehicle exhausts as well as various combustion systems.

Table 20. Representative Volume Compositions of Hydrocarbon Component of Vehicular Emissions (Schofield, 1974)

| | Reciprocating Engine, % | Rotary Engine, % |
|---|---|---|
| Methane | 24.27 | 4.88 |
| Acetylene | 17.51 | 3.30 |
| Ethylene | 14.12 | 8.09 |
| Propylene | 7.34 | 5.34 |
| Toluene | 5.97 | 16.34 |
| 1-Butene, 1,3-butadiene | 4.07 | 2.99 |
| Benzene | 2.15 | 1.31 |
| Ethane | 1.97 | 1.32 |
| 3 Ethyl pentane, 2,2,4-trimethyl pentane | 1.81 | 2.89 |
| Isopentane | 1.73 | 8.64 |
| n-Butane, 2,2-dimethyl propane | 1.59 | 4.51 |
| 2,3- and 3,3-Dimethyl hexane, 2,3,3- and 2,3,4-trimethyl pentane | 1.54 | 2.73 |
| p,m-Xylene | 1.30 | 5.57 |
| Propadiene | 1.00 | 0.95 |
| o-Xylene, phenyl ethylene (styrene) | 0.76 | 2.67 |
| cis-1-Phenyl-1-propene, t-butyl benzene, 1,2,4-trimethyl benzene | 0.76 | 2.45 |
| 2,3-Dimethyl pentane, 2-methyl hexane | 0.64 | 2.86 |
| 2-Methyl pentane | 0.55 | 1.36 |
| 1-Methyl 3- or 4-ethyl benzene | 0.52 | 2.31 |
| Ethyl benzene | 0.51 | 1.67 |
| cis-2-Butene | 0.51 | 0.25 |
| 1-Methyl-2-ethyl benzene, 2-phenyl-1-propene | 0.45 | 1.07 |
| 2,4-Dimethyl pentane, 2,2,3-trimethyl butane | 0.38 | 1.32 |
| Other paraffins | 4.07 | 6.26 |
| Other aromatics | 1.11 | 3.78 |
| Other olefins | 3.37 | 5.11 |

### c. Pyrolysis

Fisher and Neerman (1966) have identified styrene in gas products from laboratory pyrolysis of phenolic resins used in commercial brake linings for automobiles. In this study to determine compositions of brake lining resins, various resin samples were subjected to temperatures reaching 1100°C by a laboratory pyrolyzer to convert the solid samples into gaseous products which could be analyzed by gas chromatography. Detectable amounts of styrene were identified in all pyrolyzed samples.

It has been reported that brake linings in automobiles can be subject to temperatures of 800 to 1000°C (Rohl *et al.*, 1976). Under these conditions, it may be possible that small amounts of styrene are produced and thereby, emitted to the general environment.

### d. Cigarette Smoke

Both ethylbenzene and styrene have been identified in cigarette smoke condensate. Johnstone *et al.* (1962) detected ethylbenzene in cigarette smoke in yields ranging from 7 to 20 micrograms per cigarette as well as styrene, in combination with *o*-xylene, in yields ranging from 20 to 48 micrograms per cigarette.

### e. Incineration

It was previously mentioned that pyrolysis of phenolic resins can produce styrene. It is possible that municiple incineration of phenolic type resins could emit styrene. It is also conceivable that incineration of the many types of styrene polymers could release styrene to the environment.

## D. Analytical Methods

### 1. Sampling Techniques

Analytical methods have been developed for styrene and related compounds when present in solid, liquid, or gaseous substrates. The solid substrates for which there exists a significant body of literature are polystyrene and rubber samples. Sampling is relatively straightforward for solids, but more complicated for gases and liquids. The liquid substrate of greatest concern for styrene sampling is water. Recently reported techniques for the extraction of styrene from water are discussed below. Most of the environmental monitoring of styrene compounds has been done on the atmosphere, the ideal environmental medium for the containment and transport of appreciable quantities of these compounds since all the compounds are relatively volatile. In addition to the importance of air sampling as a primary method for monitoring styrene compounds in the environment, it presents certain special problems of recovery, particularly when quantitative estimates are required.

Sampling techniques are to a great extent independent of the particular analytical technique employed for determining the sample. The sampling techniques discussed in this section are therefore all generally applicable to the analytical methods in the sections which follow.

There is a much larger body of literature on sampling and analytical techniques for styrene and ethylbenzene than for divinylbenzene and α-methylstyrene. Nevertheless, the chemical and physical similarities between styrene and the other styrene monomers suggests that the sampling and analytical techniques discussed below are in most cases equally applicable, and in the balance directly adaptable to all of the styrene monomers.

Some of the earliest methods for sampling styrene in air were developed by Rowe et al. (1943) and were cited years later (Boundy and Boyer, 1952; Dow Chemical, 1960) as the basis for improved collection methods. The first of these is designed for small samples. A bead-packed absorber (see Fig. 9) filled with a suitable styrene solvent is immersed in a cold bath and the measured air sample (approximately 1 liter) is passed through it. For large samples a reflux cold trap can be used (Boundy and Boyer, 1952). This consists of a fritted glass absorber cooled by circulating around it a mixture of carbon tetrachloride and chloroform refrigerated in a dry ice bath. A third collection method, useful for spot samples of air, utilizes an evacuated flask from which styrene may be recovered with an appropriate solvent. Techniques similar to these have been employed more recently. For example, Neligan et al. (1965), in monitoring the atmosphere of Los Angeles for hydrocarbons, including styrene and ethylbenzene, collected samples in plastic bags and then transferred the samples to evacuated 2 liter glass flasks. Yamamoto and Cook (1968) used a conventional all glass fritted bubbler to monitor styrene and ethylbenzene in air. Recovery efficiency of the styrene for concentrations within 25 to 200 ppm was within 95 to 100%, but the recovery for ethylbenzene over the same concentration range was 64 to 92%.

For qualitative analysis of air, a variety of adsorbents and solvents are suitable for retaining styrene monomers and ethylbenzene. Quantitative analysis of the highest accuracy where ultratrace conditions are encountered presents a different situation. Grob and Grob (1971) assert that only charcoal filters with liquid desorption is satisfactory for ultratrace work, as these alone are capable of controlled adsorption independent of

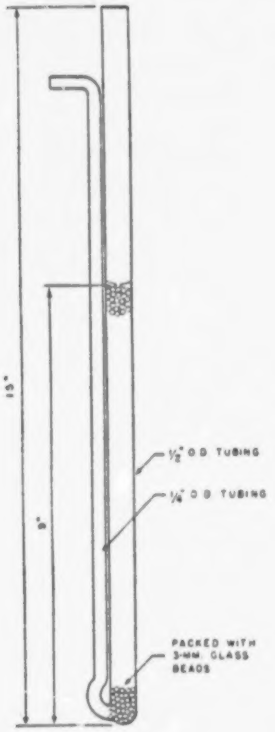

15"
9"
1/2" O D TUBING
1/4" O D TUBING
PACKED WITH
3-MM. GLASS
BEADS

Figure 9. Bead-Packed Absorber for Absorbing Styrene Monomer from Air (Boundy and Boyer, 1952)

humidity, and full recovery without contamination by material from the absorbed medium. The design of a charcoal based sampling system is shown in Figure 10. Each charcoal filter is made of 25 mg wood charcoal. The simple construction allows excellent replication of characteristics from one filter to another. The filter holder shown in Figure 10 is connected to a water pump with the air flow adjusted to 2.5 ml/min by means of a needle valve. The sample is recovered in a very low volume (ca. 0.3-0.5 ml) of carbon disulfide in the apparatus shown in Figure 11.

Activated charcoal was used by Cooper et al. (1971) to trap ethylbenzene in ambient air in an industrial environment, and by Parkes et al. (1976) for trapping styrene in ambient air. In the latter case, with carbon disulfide desorption, 40 ppb styrene in a 10 liter air sample (sampled at 200 ml/min) could be recovered with 100% efficiency.

Kalliokoski and Pfäffli (1975) developed a personal sampler consisting of batteries, pump, and a charcoal trap which is worn by a worker. Air from the worker's breathing zone is sucked through a tube into a charcoal filter. Recovery is with dimethylformamide. The range and sensitivity of the system is 5 to 1500 ppm for one hour of sampling at 0.2 ℓ/min; for a four hour sampling period at the same rate, the range is 2 to 400 ppm. Sample recovery from air with known concentrations of styrene was better than 90%. Measurement of the air flow rate proved to be the greatest source of error.

Cold trap preconcentration of air samples is a popular method of analyzing styrenes and ethylbenzene in ambient air samples where concentrations less than 1 ppb are found. A glass bead cold trap (liquid nitrogen) was used by Lonneman et al. (1968). After collection the sample was directly flushed into a gas chromatograph. Concentrations well below 6 ppb could be

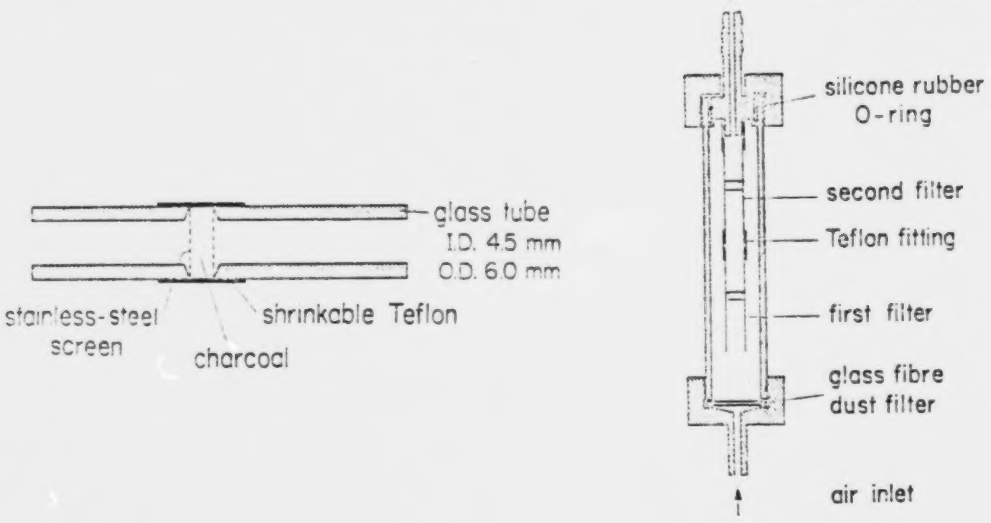

glass tube
I.D. 4.5 mm
O.D. 6.0 mm
stainless-steel screen
shrinkable Teflon
charcoal
to water pump
silicone rubber O-ring
second filter
Teflon fitting
first filter
glass fibre dust filter
air inlet

Figure 10. Design of Charcoal Filter and Filter Holder Containing Two Charcoal Filters in Series (Grob and Grob, 1971)

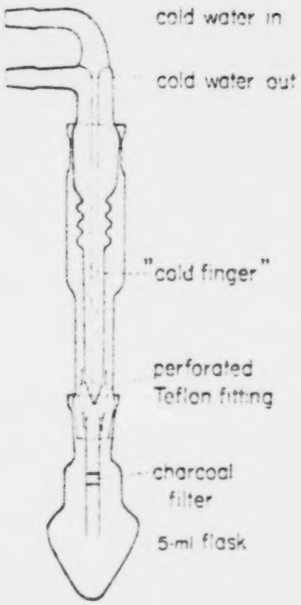

cold water in
cold water out
"cold finger"
perforated Teflon fitting
charcoal filter
5-ml flask

Figure 11. Glass Apparatus Allowing Continuous Extraction of Charcoal Filters Using a Very Low Volume of Solvent (Grob and Grob, 1971)

detected. Neligan et al. (1965) also concentrated their samples with a firebrick cold trap. A similar heat desorption technique was used by Parkes et al. (1976) with a carbon adsorbent. They were able to measure down to 1 ppb with styrene and 4 ppb with ethylbenzene.

In Sweden, personnel and ambient air samples containing styrene and styrene oxide were collected by adsorption in charcoal (Fjeldstadt et al., 1979; Pfäffli et al., 1979). The samples were then eluted with carbon disulfide or dichloromethane.

Carbon filters have also been used to sample styrene in water (Gordon and Goodley, 1971). Extraction of water samples with organic solvents such as chloroform, ether, or hexane is an alternative to charcoal filtration. Austern et al. (1975) extracted water samples with Freon-TF and were able to detect minimum levels of styrene at 0.5 and 0.3 ng respectively per water sample.

Styrene and other hydrocarbons can be removed from water samples by adsorption on macroreticular resins followed by solvent elution. Recovery is said to be excellent at ultra low levels (Bertsch et al., 1975).

Gas phase stripping is a relatively new method (Grob and Zuercher, 1976) in which a gas is bubbled through a water sample and volatile chemicals are collected on an adsorbent (wood charcoal, heat activated). It is possible to recover 0.5 ppb ethylbenzene from a liter of tap water using this technique with an extraction efficiency of 99.4% using methylene chloride as the solvent desorbent.

Table 21 summarizes the air and water sampling methods above.

### 2. Chromatographic Methods

Gas chromatography is the single most effective tool currently available for the separation of complex mixtures of organic compounds (Gordon

Table 21. Sampling Methods for Styrene Monomers and Ethylbenzene

| Method | Medium Sampled | Recovery/Efficiency | Reference |
|---|---|---|---|
| Bead-packed absorber | air | | Boundy and Boyer, 1952 |
| Glass bead cold trap | air | measure concentrations less than 6 ppb | Lonneman et al., 1968 |
| Reflux cold trap | air | | Boundy and Boyer, 1952 |
| Ambient bubbler | air | 25-200 ppm styrene/95-100%<br>25-200 ppm ethylbenzene/64-92% | Yamamoto and Cook, 1968 |
| Evacuated container | air | | Boundy and Boyer, 1952 |
| Plastic bag | air | | Neligan et al., 1965 |
| Carbon filter | air | | Grob and Grob, 1971 |
| Carbon filter | air | | Cooper et al., 1971 |
| Carbon filter/solvent desorption | air | | Fjeldstad et al., 1979<br>Pfäffli et al., 1979 |
| Carbon filter/heat desorption | air | 40 ppb styrene/100% | Parkes et al., 1976 |
| Carbon filter | water | | Gordon and Goodley, 1971 |
| Solvent extraction | water | 0.5 ng styrene/sample<br>0.3 ng ethylbenzene/sample | Austern et al., 1975 |
| Macroreticular resins | water | | Bertsch et al., 1975 |
| Gas phase stripping | water | 0.5 ppb ethylbenzene/99.3% | Grob and Zuercher, 1976 |

and Goodley, 1971). It is also the most common tool mentioned in the literature for determining styrene and ethylbenzene in the air and water samples as well as residual amounts of styrene in polymers.

A typical example of routine gas chromatography applied to ethylbenzene monitoring was a study of the Los Angeles atmosphere by Altshuller and Bellar (1963). Ethylbenzene was detected in the air samples by directly injecting 3.12 ml of air into a gas chromatograph equipped with a flame ionization detector. Concentrations down to 0.005 ppm were measured. The lower limit of sensitivity of the apparatus was not given.

Neligan _et al_. (1965) also monitored the Los Angeles area atmosphere, performing analyses with a modified flame ionization gas chromatograph using a copper capillary coated column. Extensive sample preparation included drying with Ascarite, freeze-out trap collection at liquid oxygen temperatures, and rapid vaporization prior to injection. Recovery of hydrocarbons from spiked air was reproducible within ±10% at the 0.1 ppm level and ±25% at the 0.001 ppm level. Ethylbenzene and styrene were detected along with 18 other aromatics in air samples analyzed. Fjeldstad _et al_. (1979) and Pfäffli _et al_. (1979) both used gas chromatography flame ionization detection for detection of styrene and styrene oxide in charcoal collected samples taken around plastics industries using styrene monomer. Pfäffli _et al_. (1979) used a capillary column and confirmed the qualitative results with GC-MS. The detection limits for the two studies were around 3 ppb.

Ethylbenzene was detected in the atmosphere over Zurich, Switzerland in an application of ultratrace analysis on capillary columns via gas-liquid chromatography/mass spectrometry (Grob and Grob, 1971). Samples were collected using the charcoal filters described in the previous section (see Fig. 10). These were extracted with carbon disulfide and analyzed with specially modified gas chromatography columns, followed by mass spectrometry. It was shown that charcoal does not attain a stable equilibrium in prolonged contact with the atmosphere. Less volatile substances are capable of replacing the more volatile substances on prolonged exposure of filters to air. Consequently there is an optimum exposure time for charcoal filters for maximum sample retention. Ethylbenzene concentration in Zurich air was 8.7 ppb. No lower limit of detection was given, but similar molecules were detected at much lower levels (e.g., ethyldimethylbenzene at 0.95 ppb). A further refined system (again using gas-liquid chromatography/mass spectrometry) was able to detect hundreds of hydrocarbons up to $C_{24}$ in Zurich tap water after they were stripped from water onto an adsorbent (Grob, 1973). The lower limit of sensitivity was found to be 0.1 ppt. Routine assays on the order of 5 ppt are possible with errors on the order of 25%. Errors tend to be on the low side due to failure to recover all of the sample from the collector (Grob, 1973).

Bergert et al. (1974) developed another ultratrace system employing gas chromatography/mass spectrometry which was used to analyze ambient air collected in Frankfurt-am-Main, Germany, for hydrocarbons, including ethylbenzene. A microgradient tube is used for enrichment of the components. Separation is carried out on glass thin-film open tubular columns by means of linear-programmed low temperature gas chromatography. Combined with mass spectrometry, this system can detect components down to 0.02 ppb, but the usual range of operation is 0.1 ppb to 1.0 ppm.

Louw and Richards (1975) reported a gas chromatography/infrared spectroscopy system for low molecular weight hydrocarbons. Each sample component is identified in five to six minute intervals. Approximately 14-19 μg of each hydrocarbon component must be present per sample. At the time of publication of the method, however, it had not yet been tested with actual urban air samples.

In addition to air pollution monitoring, gas chromatography has been used to determine styrene, ethylbenzene, and other organics in water. Austern et al. (1975) developed a method for extracting wastewater samples with Freon-TF, then used standard gas chromatographic techniques to show the extraction technique is capable of recovering approximately 99% of styrene and ethylbenzene when these are present in concentrations of about 0.25 mg/ℓ.

Gas chromatography was also used to detect ethylbenzene and styrene in commercial deionized charcoal-filtered water by first air stripping the organics, collecting them on a solid polyphenyl ether adsorbent, and then thermally stripping them onto a capillary column (Dowty et al., 1975). In this case the gas chromatography was followed by mass spectrometry in a computer controlled system for identification and quantification of organics in water. Concentration of ethylbenzene and styrene were not reported.

Bertsch et al. (1975) used a system similar to Grob and Grob (1971) to sample ethylbenzene in river water. Although quantitative data were not presented, it can be inferred the apparatus is capable of ultratrace analysis to the ppb level.

Parkes et al. (1976) used a relatively simple charcoal adsorption/heat desorption technique to concentrate organics in air and determine them via flame ionization gas chromatography. Heat desorption was accomplished with a Bendix Flasher which rapidly heats the sample trap from ambient to several hundred degrees, volatilizing the organics. Parts per billion sensitivities are easily achieved with this method with a total analysis time of about 20 to 40 minutes per sample.

Hoshika (1977) reported a gas chromatography method which does not require preconcentration of the samples, even when the styrene is at the ppb level (which is too low for flame ionization detection without preconcentration). The styrene is converted to styrene dibromide by reacting it with bromine. The dibromide is detected with an electron capture detector. The electron capture system was shown to be 500 times more sensitive to styrene bromide than a flame ionization system to styrene. Of 138 compounds tested for interference effects on the bromination of styrene, all except six compounds proved to have negligible effect (error < 5%). The six and the respective % errors introduced into the height of the styrene dibromide chromatographic peak were 1-nonene (19%), 1-dodecene (100%), _o_-cresol (150%), _m_-cresol (45%), 2,3-xylenol (20%), and 3,5-xylenol (20%). The phenolic compounds could be removed with base. Recovery of the styrene from air samples spiked with 13 ppb styrene was about 90%. The range of the styrene detected in urban air samples was 0.1 to 0.4 ppb.

Reichel _et al_. (1977) used gas chromatography/mass spectrometry to determine polychlorinated styrenes (octachloro and possibly also hexa and heptachlorostyrenes) in heron tissues. This routine application of GC/mass spectrometry achieved a sensitivity of at least 0.01 ppm.

The requirement for the high sensitivities exhibited by the previously described systems does not exist for assays designed to detect styrene monomers in polymer substrates. Thus, Shapras and Claver (1964) determined styrene and ethylbenzene in various styrene polymers and copolymers using gas chromatography with a hydrogen flame detector, reporting a sensitivity of 10 ppm monomer in the polymer. Esposito and Swann (1965) developed a technique for the determination of styrene monomer in polyester resins by gas-liquid chromatography. The styrene monomer is used as a consolidating agent in the resins; regulation of styrene concentration is important in determining the properties of the resin product. The procedure has good precision for styrene resins in at least the concentration range of 12 to 47%. It is not relevant to environmental monitoring. Haken and McKay (1966) reported another procedure for styrene in polyester resins via gas chromatography. No sensitivity data was given.

Table 22 summarizes the chromatographic analytical methods for styrene described above.

### 3. Spectroscopic Methods

Analytical methods employing ultraviolet spectroscopy (without gas chromatography) were primarily developed for determining styrene monomers in polymer products. The spectroscopic method developed by Yamamoto and Cook (1968), however, was for styrene in air. Spectroscopic methods are rapid and require a minimum amount of apparatus. However, they cannot compete with the sensitivity achievable with gas chromatography. Also, ultraviolet methods usually cannot distinguish between various volatile substances in polystyrene when more than one is present, such as other copolymers or stabilizers (Crompton et al., 1965).

Some UV methods depend on the fact that the unsaturated side chain of styrene causes an absorption below 260 mμ while polystyrene has an absorption above 260 nm. In these cases a solvent must be chosen which will dissolve both the monomer and polymer. Murphy and Forrette (1961) avoided this problem by extracting styrene from polystyrene with cyclohexane then measuring the monomer at 250 nm. Data on the sensitivity and concentration range of the method were not given. A similar method (Rose, 1965) is said to be able to

Table 22. Chromatographic Analytical Methods for Styrene Monomers and Ethylbenzene

| Method | Compound(s) | Source | Sensitivity | Reference |
|---|---|---|---|---|
| Gas Chromatography-FI (direct injection) | ethylbenzene | atmosphere | >0.005 ppm | Altshuller and Bellar, 1963 |
| Gas Chromatography - FI | ethylbenzene, styrene | styrene polymer | >10 ppm | Shapras and Claver, 1964 |
| Gas Chromatography-FI (cold trap) | ethylbenzene, styrene | atmosphere | >0.01 ppm | Neligan et al., 1965 |
| Gas Chromatography | styrene | polyester resins | ND | Haken and McKay, 1966 |
| Gas Chromatography - FI | styrene | * | 0.2 ppb | Parkes et al., 1976 |
| Gas Chromotography-FI | styrene<br>styrene oxide | atmosphere | 3 ppb | Fjeldstad et al., 1979 |
| Gas Chromotography-FI (also GC-MS) | styrene<br>styrene oxide | atmosphere | <40 ppb | Pfäffli et al., 1979 |
| Gas Chromatography - EC | styrene as the dibromide | atmosphere | 0.1 ppb | Hoshika, 1977 |
| Gas/Liquid Chromatography | styrene | polyester resins | ND | Esposito and Swann, 1965 |
| Gas/Liquid Chromatography/Mass Spectroscopy | ethylbenzene<br>ethylbenzene | atmosphere<br>potable water | >1 ppb<br>~0.1 ppt | Grob and Grob, 1971<br>Grob, 1973 |
| Gas Chromatography/Infrared Spectroscopy | ethylbenzene | * | ND | Louw and Richards, 1975 |
| Gas Chromatography/Mass Spectroscopy | ethylbenzene | atmosphere | 0.02 ppb | Bergert et al, 1974 |
|  | polychlorinated styrenes | heron tissue | >0.01 ppm | Reichel et al., 1977 |

---

* Method developed with synthetic mixtures of air and hydrocarbons, but applicable to atmospheric monitoring.

ND No data reported.

detect as little as 0.02% monomer in food grade polystyrene. Apart from what may be a safe level of monomer in polymers used for food packaging, levels of styrene monomer above 0.25% may impart a definite odor to foods (de Forero et al., 1971).

Yamamoto and Cook (1968) extracted styrene and ethylbenzene from air samples by drawing them through spectro-grade octane. The styrene in the samples was directly determined by UV spectroscopy at 268 nm and ethylbenzene at 291 nm. These wavelengths were chosen for minimal (or at least compensable) cross interference between the two compounds. Tested with spiked samples, the method proved capable of determining styrene at levels of 25 to 200 ppm with about 95% efficiency or better (including extraction). Ethylbenzene reproducibility was not as good, with efficiency of the method for ethylbenzene ranging nonlinearly from 65 to 92% over the same concentration range. Styrene interfered significantly with the ethylbenzene when the concentration of the ethylbenzene fell below half that of the styrene. The method can detect styrene and ethylbenzene concentrations as low as 1 ppm.

### 4. Electrochemical and Miscellaneous Methods

Although the polarography of styrene was investigated in the early 1940's, interest in this technique for analysis of styrene took time to develop. Ragelis and Gajan (1962) extracted styrene from polystyrene resin, then used polarography to determine the styrene. Their results agreed well with gas chromatography analyses of the same samples. Sensitivity data was not given, but Crompton and Buckley (1965) reported sensitivities as low as 20 ppm in the determination of styrene in styrene-acrylonitrile copolymers via polarography. Results of the polarographic method agreed well with those of UV spectroscopy at 292 nm.

Using the effect of organic impurities on the double layer capacitance of an electrode, Formaro and Trasatti (1968) were able to detect as little as 0.03 ppm of organic impurities in water. Among the compounds present was styrene. The method, however, is nonspecific. It gives a measure of the total organic impurities present. It is applicable to industrial wastewater quality control as well as to tap water monitoring for organic pollution.

Blake and Rose (1960) described a colorimetric method for styrene and toluene in air samples. A bulb is inflated with the air to be tested. Styrene in the sample reacts with an 89.5% solution of sulfuric acid producing a colored solution. The sample bulb is inflated as many times (between 3 - 10) as necessary until the reagent solution is the same color as a standard solution. The concentration of styrene in the sample is proportional to the number of inflations required. The test is very rapid, but limited in range and sensitivity (approximately 50 to 170 ppm). It is nevertheless suitable for spot checks in enclosed areas with the potential for undesirably high styrene levels. A similar method for homologs of benzene was described by Belvedere and Metrico (1967), but this method is not highly specific for styrene; sensitivity data was not given.

The classical chemical method for styrene was the nitration method (Boundy and Boyer, 1952). The monomer, which was collected in a bead-packed absorber, is nitrated with a mixture of concentrated sulfuric and nitric acids after removal of butadiene (if present) by heating. The nitrated product is diluted to volume with water and determined by measuring the color of the solution with a photoelectric colorimeter. This method is suitable for samples containing styrene in the presence of acrylonitrile, water, butadiene, ethylbenzene, and benzene. Its accuracy is ±15 mg (roughly 1000 ppm). Methylstyrenes, divinylbenzenes, and other compounds with unsaturated side chains and which are less volatile than styrene would interfere.

A recent titrametric method for styrene (Roy, 1977) comes closest of the chemical methods to suitability for trace analysis of styrene. Its sensitivity is about 5 ppm. The monomer is extracted from styrene-acrylonitrile polymer with benzene, then brominated under conditions which do not favor bromination of the less active double bond of acrylonitrile (the two compounds may thus be determined in the presence of each other). The results for the determination of styrene monomer in styrene-acrylonitrile polymer samples which contained about 1% monomer agreed very well with infrared analyses for styrene on the same samples.

## E. Monitoring

### 1. The Atmosphere

Styrene and ethylbenzene have been monitored in the atmosphere over the west coast of the United States, and also in Europe and Japan. Ethylbenzene is apparently more prominent in the atmosphere than styrene; it has been determined more frequently and in higher concentrations than styrene in all of the following studies.

In a survey done in September 1961, Altshuller and Bellar (1963) found approximately 0.01 ppm ethylbenzene in the air over Los Angeles, California. The total aromatic concentration was approximately an order of magnitude greater; therefore, the ethylbenzene represented about 10% of the total aromatic compounds detected in the air, and roughly 1% of the total carbon compounds detected. The authors noted that only a small number of the compounds detected are active in smog-producing reactions, the majority being inert to such reactions. The total concentration of aromatic compounds in the Los Angeles air had not changed five years later when a new study was undertaken by Lonneman _et al_. (1968). The ethylbenzene concentration averaged 0.006 ppm in the more recent study (with the highest measured concentration of ethylbenzene at 0.022 ppm), indicating that its concentration (like that of the total aromatics) did not change significantly over that five year period of time. (The most abundant aromatic detected was toluene. At 0.04 ppm, toluene was twice as abundant as benzene or _m_-xylene, the two compounds which immediately followed toluene in abundance.) The ethylbenzene concentrations reported by Lonneman _et al_. (1968) and Altshuller and Bellar (1963) agree also with the data of Neligan _et al_. (1965) who monitored five different sites in California (see Table 23), including Los Angeles, reporting an average of 0.01 ppm ethylbenzene. The Neligan group also detected styrene at four of these sites (see Table 23) at an average concentration of 0.005 ppm. The reproducibility of the analytical procedure was ± 25 percent at 0.001 ppm. If there was any styrene in the air at Los Angeles, it was below the limit of detection (0.0005 ppm).

Grob and Grob (1971) found 8.7 ppb ethylbenzene in the air in Zurich, Switzerland. Styrene was not detected. The lowest concentration of any of the other detected hydrocarbons was 0.74 ppb for ethyldimethylbenzene. Toluene was not only the most abundant of the aromatics, but, at 39 ppb, also the most abundant hydrocarbon of all those detected. The authors noted the striking resemblance of the kinds of compounds detected and their relative abundance in the composition of gasoline. The alkanes in air were slightly reduced in concentration compared to the aromatics over what one would expect for gasoline.

Table 23. Styrene and Ethylbenzene Concentrations (ppm V/V) in California Air Samples (Neligan _et al._, 1965)

| | Inglewood | | Long Beach | | Burbank | | Azusa | | Los Angeles | |
|---|---|---|---|---|---|---|---|---|---|---|
| Time (PST) | 0700 | 0730 | 0700 | 0730 | 0600 | 0900 | 0900 | 1000 | 0600 | 0700 |
| Styrene | 0.008 | 0.015 | 0.002 | 0.001 | 0.002 | 0.003 | 0.004 | 0.005 | not detectable | |
| Ethylbenzene | 0.011 | 0.013 | 0.006 | 0.012 | 0.005 | 0.008 | 0.004 | 0.004 | 0.014 | 0.015 |

In November 1973, ethylbenzene was detected in the air of Frankfurt-am-Main, Germany (Bergert et al., 1974) at roughly 1 ppb. More than twenty other hydrocarbons were monitored at the same time. Styrene also has been found in urban air in Japan at a concentration of 0.2 ppb (Hoshika, 1977). It is possible that Neligan et al. (1965) would have detected styrene at about this concentration in Los Angeles if their analytical method had been sufficiently sensitive.

Olivo et al. (1973) have shown that industrial activity may contribute to styrene contamination of the atmosphere. The working areas of a plastics plant in Italy were monitored. Styrene concentration in the air of molding rooms frequently exceeded the maximum allowable concentrations. Pervier et al. (1974) note that although styrene has been monitored in the vent emissions of petrochemical plants in this country, the quantities involved are not significant compared to other polluting processes (see Section II-C for a discussion of the environmental contamination potential of styrene). Two Swedish studies have detected considerable concentrations of styrene and styrene oxide in air samples collected at polyester resin plants (fiber glass lamination). Concentrations of 50-150 ppm styrene and 0.03 - 0.2 ppm styrene oxide were detected (Pfäffli et al., 1979; Fjeldstad et al., 1979).

In summary, the available data from the West Coast, Switzerland, Germany, and Japan indicates that ethylbenzene is significantly more abundant than styrene in the atmosphere. While industrial processes may be one source of these compounds, the suggestion has been raised that their presence might also be attributable to the widespread use of gasoline (see Table 20). Table 24 summarizes the atmospheric monitoring data for styrene and ethylbenzene.

Table 24. Atmospheric Monitoring Data for Styrene and Ethylbenzene

| Compound | Location | Approximate Average Concentration | Reference |
|---|---|---|---|
| Styrene | California* | 0.005 ppm | Neligan *et al*., 1965 |
| Styrene | Urban air (Japan) | 0.2 ppb | Hoshika, 1977 |
| Ethylbenzene | Los Angeles, California | 0.01 ppm | Altshuller and Bellar, 1963 |
| Ethylbenzene | Los Angeles, California | 0.01 ppm | Lonnemann *et al*., 1968 |
| Ethylbenzene | California* | 0.01 ppm | Neligan *et al*., 1965 |
| Ethylbenzene | Zurich, Switzerland | 8.7 ppb | Grob and Grob, 1971 |
| Ethylbenzene | Frankfurt-am-Main, Germany | ∼1 ppb | Bergert *et al*., 1974 |

---

* See Table 23 for details of the five locations.

No data has been encountered for either α-methylstyrene or divinylbenzene in the atmosphere.

2. Water

Tables 25 and 26 summarize data collected by the Environmental Protection Agency in 1976 and published in December of that year on styrene and ethylbenzene monitored in water (Shackelford and Keith, 1976). The tables show that styrene has been most frequently noted in industrial effluents, ethylbenzene in potable water. Also, there are more observations of ethylbenzene than styrene, which is the same situation for the atmospheric monitoring reported in the previous section. To account for this one would have to consider the reactivity and solubility differences of the two compounds as well as the possibility of differences in the number and types of potential sources (see Section II-C).

Keith (1972) monitored the contents of seven different industrial aqueous effluents, identifying a total of 33 different compounds in them. Styrene was found in the effluent of a petrochemical plant in which it was neither a raw material nor a product. Styrene was also found in the effluent of a synthetic rubber plant in which it was used as a raw material. Quantitative data was not given. The analytical technique used (gas chromatography/mass spectrometry) is easily capable of sub ppm sensitivity (see Section II-D).

Most of the water monitoring where concentrations were reported involved potable water. One of the most detailed cases of styrene contamination of potable water was documented by Grossman (1970). Sometime between 1959-1961, two drums of styrene had been buried beneath one to four feet of landfill at Gales Ferry, Connecticut at the conclusion of construction of a one-family housing project. In 1962 six water wells in the area began

Table 25. Styrene Identified in Water (Shackelford and Keith, 1976) (Monitoring dates, where available, are indicated in parentheses)

---

1. Effluent from a latex plant (3/74), Louisville, Kentucky
2. Effluent from a chemical plant (3/74), Louisville, Kentucky
3. Effluent from a latex plant (10/75), Calvert City, Kentucky
4. Effluent from a chemical plant (8/75), Calvert City, Kentucky
5. River water (10/75), Water Research Center, Stevenage, Hertfordshire SG1, England
6. Effluent from a chemical plant (8/74), Colliersville, Tennessee
7. Finished drinking water (1970), Mississippi River, Louisiana, EPA Report, Region VI, Dallas, Texas, April, 1972
8. Effluent from a chemical plant (1970), Mississippi River, Louisiana, *ibid*.
9. Effluent from a textile plant (1970), Mississippi River, Louisiana, *ibid*.
10. Effluent from a chemical plant (8/73), Webb, Garrison, Keith, and McGuire, EPA, Athens, Georgia
11. Finished drinking water (1/76), Bob Tardiff, EPA, Cincinnati, Ohio
12. Finished drinking water, Indiana, "Identification and Analysis of Organic Pollutants in Water," L.H. Keith, ed., Ann Arbor Science Publishers, June, 1976
13. Effluent from a textile plant (2/75), M. Gordon, personal communication, Murray State University, Murray, Kentucky
14. Effluent from a chemical plant (8/74), Memphis, Tennessee
15. Finished drinking water (8/75), Grand Forks, North Dakota, "Preliminary Assessment of Suspected Carcinogens in Drinking Water," EPA Report to Congress, December, 1975
16. Finished drinking water, New York, *ibid*.
17. River water (7/75), G.A. Turk and A.E. Stanley, Ames Lab, ERDA, Iowa State University, Ames, Iowa
18. Finished drinking water (7/75), *ibid*.
19. Effluent from a chemical plant, World Health Organization

---

Table 26. Ethylbenzene Identified in Water (Shackelford and Keith, 1976)
(Monitoring dates, where available, are indicated in parentheses)

---

1. Finished drinking water (6/71), *Anal. Chem.*, *44*, 139 (Burnham *et al.*, 1972)
2. Finished drinking water (10/75), Water Research Center, Stevenage, Hertfordshire SG1, England
3. River water (10/75), *ibid.*
4. Well water (10/75), *ibid.*
5. River water (11/73), *Chromatog.*, *7*, 118 (1974)
6. Effluent from a chemical plant (8/74), Colliersville, Tennessee
7. Finished drinking water (1970), Mississippi River, Louisiana, EPA Report, Region VI, Dallas, Texas, April, 1972
8. Effluent from a chemical plant (1970), *ibid.*
9. Effluent from a sewage treatment plant (2/76), Contract 68-01-3234, Progress Report #2, University of Illinois, Champaign, Illinois
10. Effluent from raw sewage (2/76), *ibid.*
11. Raw water (2/76), *ibid.*
12. Effluent from a sewage treatment plant (8/72), A.W. Garrison, personal communication, EPA, Athens, Georgia
13. Finished drinking water (1/76), Bob Tardiff, EPA, Cincinnati, Ohio
14. Finished drinking water (5/73), *J. Chromatog.*, *84*, 255 (1973) (Grob, 1973)
15. River water (5/75), *ibid.*, *112*, 701 (1975) (Bertsch *et al.*, 1975)
16. River water, *ibid.*, 715
17. Effluent from a sewage treatment plant, "Identification and Analysis of Pollutants in Water," L.H. Keith, ed., Ann Arbor Science Publishers, June, 1976
18. Finished drinking water (2/75), Philadelphia, Pennsylvania, *ibid.*
19. River water, Switzerland, *ibid.*
20. Effluent from a textile plant (2/75), M. Gordon, personal communication, Murray State University, Murray, Kentucky
21. Effluent from a chemical plant (8.74), Memphis, Tennessee
22. Finished drinking water, New Orleans, Louisiana
23. Finished drinking water (8/75), "Preliminary Assessment of Suspected Carcinogens in Drinking Water," EPA Report to Congress, December, 1975
24. Finished drinking water (8/75), Grand Forks, North Dakota, *ibid.*
25. Finished drinking water, New York, *ibid.*
26. River water (7/75), G.A. Junk and S.E. Stanley, Ames Lab, ERDA, Iowa State University, Ames, Iowa
27. Well water (7/75), *ibid.*
28. Finished drinking water, Zurich, Switzerland

delivering water with an obnoxious odor. The odor was due to the presence of 0.1 to 0.2 mg/ℓ styrene. In 1961-62 all known contaminating material was removed from the ground and activated charcoal filters installed on the wells. The styrene concentration (sampled ahead of the filters) began to decline and was undetectable after 1964. Data collected over the period showed that styrene may persist for at least two years after the removal of the contaminating sources under the geological conditions of the area. Despite the fact that styrene is only slightly soluble in water, it can be easily transported via water systems from one bedrock unit or subunit to another.

In another case of contaminated well water (Burnham et al., 1972), 15 ppb ethylbenzene was monitored in a well in Ames, Iowa. An objectionable taste and odor in the well water led to the testing which confirmed the presence of a variety of organics, believed to be tar residues from a coal gas plant operated in the city of Ames in the 1920's. The tar residues were buried in a pit hydrologically connected to the aquifer supplying the city's water.

Styrene has been monitored in river water in the Lower Tennessee River (Gordon and Goodley, 1971). Ethylbenzene has been monitored in the Black Warrior River (Tuscaloosa, Alabama) (Bertsch et al., 1975). Concentration data were not provided in either case.

Ethylbenzene has been monitored in the tap water of at least two major cities. Grob (1973) reported ethylbenzene in the tap water of Zurich, Switzerland as well as in the lake which is the source of Zurich's water supply. Dowty et al. (1975) found ethylbenzene, among 60 to 70 other organics, in commercial deionized charcoal-filtered water whose source was the water of New Orleans, Louisiana. Such commercial deionized filtered water is used for, among other things, the preparation of carbonated beverages. Specific quantitative data were not given.

The water monitoring discussed above is summarized in Table 27.

### 3. Food and Other Ingested Materials

Styrene has been monitored in food products and also in several other non-nutritive materials which humans may ingest. Polystyrene food packaging is a potential source of styrene monomer which may migrate into the food contained in the package. Container manufacturers have an impetus to keep monomer levels extremely low, not only because of the potential hazards involved in the ingestion of the monomer, but also because styrene imparts very undesirable odors to food at relatively low concentrations. For example, styrene can be detected in milk at 0.5 ppm and imparts a disagreeable odor and flavor to yogurt at 0.2 ppm (Jensen, 1972). Finley and White (1967) monitored styrene in milk stored in polystyrene containers for up to eight days (presumably under refrigeration, although storage conditions were not specified). They were unable to detect styrene in the milk. The lower limit of sensitivity of their analytical method was 0.05 ppm. By current standards this is not especially sensitive. It was not indicated how much, if any, residual styrene monomer was actually present in the plastic containers which were used in the experiment.

Kinlin et al. (1972) found both styrene and ethylbenzene in roasted filbert nuts, along with 227 other organic compounds. Neither had been previously reported in roasted filberts. No quantitative data were given. The nut samples were not unusual in any way. The aim of the analyses was to identify molecules contributing to the characteristic filbert flavor rather than to seek contaminants.

Table 27. Styrene and Ethylbenzene Monitored in Water

| Compound | Location | Medium Monitored | Concentration | Reference |
|---|---|---|---|---|
| Styrene | petrochemical plant | effluent | no data | Keith, 1972 |
| Styrene | synthetic rubber plant | effluent | no data | Keith, 1972 |
| Styrene | southeastern Connecticut | well water | ∿1 ppm | Grossman, 1970 |
| Styrene | Lower Tennessee River | river water | no data | Gordon and Goodley, 1971 |
| Ethylbenzene | Ames, Iowa | well water | no data | Burnham *et al.*, 1972 |
| Ethylbenzene | Tuscaloosa, Alabama | river water | no data | Bertsch *et al.*, 1975 |
| Ethylbenzene | Zurich, Switzerland | tap water | no data | Grob, 1973 |
| Ethylbenzene | New Orleans, Louisiana | commercial deionized charcoal-filtered water | no data | Dowty *et al.*, 1975 |

Styrene has been found in four of seven samples of whiskey screened for organics (Kahn et al., 1968). Two Bourbon samples (3 and 4 years old) and one Canadian (unaged) sample of the seven did not contain styrene, whereas one other Bourbon and two other Canadian whiskey samples (all unaged) and the condensate from a conventional beer still all contained styrene. Quantitative data were not given.

Styrene is a component of cigarettes and cigarette smoke. Baggett et al. (1974) found 18 μg of styrene per cigarette in a domestic filter blend. In addition, styrene was identified in the smoke. Styrene was also found in the air of an unventilated smoking chamber after a machine had smoked 30 American blend cigarettes (Jermini et al., 1976). The concentration of the styrene was approximately 0.026 ppm.

Withey and Collins (1978) have recently conducted a detailed study of styrene in polystyrene packaging and food in contact with packaging. Levels of styrene monomer in polystyrene food containers varied from 30 to 210 ppm (limit of detection was 1 ppm). The concentrations in a variety of dairy products ranged from 20-80 ppb in yogurt (limit of detection was 0.91 ppb) to 140-240 ppb in sour-cream (limit of detection was 13.4 ppb). The concentration in food containers is well within FDA standards (10,000 ppm).

4. Industrial Products

Styrene and ethylbenzene have been reported in certain industrial products in which their presence, if not surprising, might not necessarily be expected. Styrene, for example, was found in brake lining pyrolysis products (Fisher and Neerman, 1966), which suggests that the wearing of brake linings may be a minor source of styrene in the atmosphere. Esposito (1968) found ethylbenzene in a variety of industrial aromatic solvents and synthetic mixtures, many of whose formulas are proprietary. Stavinoha and Newman (1972) found ethylbenzene in regular and premium grade gasolines. Gasoline has been suggested (Grob and Grob, 1971) as a possible source for ethylbenzene in the atmosphere (see Section II-C).

### 5. Miscellaneous Monitoring

Reichel et al. (1977), analyzing estuarine bird samples collected in 1970 and 1973 from the Lake St. Clair, Michigan area, found polychlorinated styrenes in carcass and egg tissues of the Great Blue Heron (Ardea herodias). Octochlorostyrene was detected at 0.4 ppm in two of three samples of carcass. An average of 0.1 ppm was found in three of four samples of egg. Heptachloro and hexachlorostyrenes were tentatively identified in the tissues as well. The source of polychlorinated styrenes in these environmental samples is not known. Since these are not commercially important chemicals, they may have been formed in the environment by some as yet unknown mechanism from unknown precursors.

# III. Health and Environmental Effects

## A. Environmental Fate and Transport

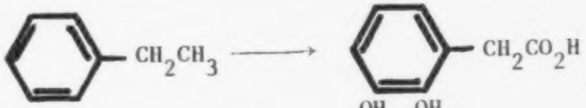
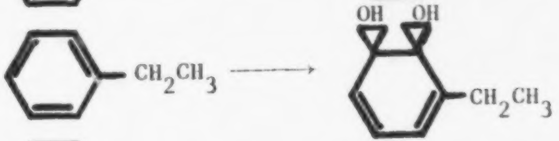
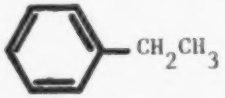
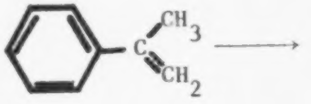
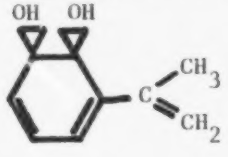
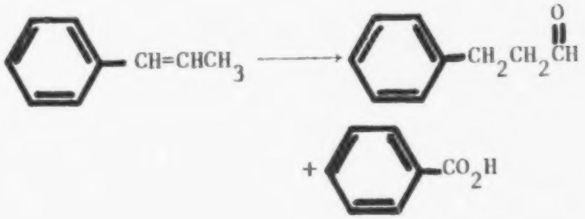
### 1. Biodegradation

Both ethylbenzene and styrene appear to be susceptible to metabolism with mixed cultures of microorganisms. Ludzack and Ettinger (1963) examined the degradation of ethylbenzene (19 to 25 mg/ℓ) in Ohio River water using 5 gallon carboys over a period of 35 days. They measured the carbon dioxide (unlabelled) evolution compared to a control and reported their results as percent of theoretical. Ethylbenzene did not reach more than 50% of theoretical over 35 days, but part of the carbon was suspected to have been lost by volatilization. Similar results were found by Pahren and Bloodgood (1961) for styrene and a variety of vinyl compounds. McKinney *et al*. (1956) showed that phenol activated sludge was able to remove 27% of the theoretical oxidation of 500 ppm of ethylbenzene in 12 hours of aeration.

Price and coworkers (1974) conducted 20 day BOD tests on styrene at 3, 7, and 10 mg/ℓ. Their results were corrected for nitrification and reported as percent of theoretical BOD. In 20 days, styrene had reached 85% of theoretical while benzene was 20% and phenol was 95%.

Several studies have attempted to determine the pathways of microbial metabolism of ethylbenzene and α-methylstyrene using pure cultures. These studies are summarized in Table 28. In general, it appears that oxidation can occur on the ring (cis-dihydroxylation) and on the side chain. When the alkane or alkene is a straight chain, attack on the chain is favored; when it is branched (α-methylstyrene), cis-dihydroxylation on the ring appears to be favored.

Table 28. Pure Culture Metabolism of Ethylbenzene and α-Methylstyrene

| Reference | Microorganism | Results |
|---|---|---|
| Davis and Raymond, 1961 | Nocardia sp. |  |
| Gibson and Yeh, 1973 | Pseudomonas putida 39/D |  |
| Gibson *et al.*, 1973 | Pseudomonas putadia |  - used as growth substrate |
| Omori *et al.*, 1974 | bacteria (unknown)<br>isolated from soil<br>by enrichment on<br>isopropylbenzene |  <br> |

Recently, Grbić and Munjko (1977) examined the ability of streptomycetes isolated from soil and river water to utilize styrene and α-methylstyrene as a sole carbon source. None of the soil strains were able to grow, but four (80%) of the river water strains could grow on the chemicals.

Guillet et al. (1974) studied the biodegradability of a photodegraded polystyrene-vinyl ketone copolymer. Their result indicated that after photolysis small amounts (<0.20%) of $^{14}CO_2$ are evolved from both a soil and activated sludge environment. However, these results provide little insight into the biodegradability of the styrene monomer.

### 2. Chemical Degradation

The available information on environmental chemical reactions has already been reviewed in Section I-B. In general, the styrene compounds are very susceptible to oxidation processes and under smog conditions react very rapidly. Ethylbenzene is less reactive under smog conditions but is one of the more reactive hydrocarbons studied. None of the compounds is expected to hydrolyze in the environment.

### 3. Environmental Transport

The physical properties (Table 2) of the styrenes and ethylbenzene suggest that they are relatively volatile and are soluble in water at trace quantities. Both ethylbenzene and styrene have been detected in ambient water and air samples. The high vapor pressure of styrene (4.53 torr at 20°C) and ethylbenzene (38.60 torr at 20°C) suggests that these compounds will exist in the vapor state in the atmosphere and, depending upon how fast they degrade, could be carried long distances.

These compounds in water are not likely to bioconcentrate in biological organisms because of their relatively high water solubilities.

Using the water solubilities of ethylbenzene (200,000 ppb) and styrene (290,000 ppb) and the equation of Metcalf and Lu (1973), the biomagnification factor is 16 and 12, respectively.

The evaporation half-life of the compounds from water can be calculated from the molecular weight, water solubility, and vapor pressure (Dilling, 1977). The half-lives for styrene and ethylbenzene assuming a water depth of one meter are 23.8 hours and 7.5 hours, respectively.

Some information is available which suggests that these compounds do leach through soil. In research oriented at stabilizing soil columns with resins in order to optically observe the soil, Wells (1963) found that liquid styrene monomer moved readily through the column.

Grossman (1970) documented an incident where at least two left-over drums of waste styrene that were buried 1 to 10 feet deep allowed the migration of the chemical into bedrock aquifers that were being used for drinking water. The styrene moved downward with water through the glacial till and into the aquifer. The contamination persisted at least 2 years after removal of the buried sources. Styrene migrated at least "300 feet along joints into cones of depression resulting from small-scale pumping for individual family dwellings." The styrene had been used to burn brush in clearing land for the development.

## B. Biological Effects

### 1. Toxicity and Clinical Studies in Man

### a. Occupational Studies

### (1) Biological Monitoring

A primary concern in evaluating the effects of styrene on man is to first define the intensity of exposure. Biological monitoring of workers exposed to styrene has, for the most part, consisted of determining the levels of styrene metabolites in urine. However, analysis of styrene in the breath, fat, and blood has also been employed in quantitating the extent of exposure.

Determination of the styrene metabolites, phenylglyoxylic, mandelic, and hippuric acids in urine has been most extensively evaluated as an index of exposure. Nevertheless, total agreement has not been reached with regard to the metabolite which best correlates with exposure intensity or duration. Ohtsuji and Ikeda (1970) observed that at styrene concentrations up to 30 ppm, mandelic and phenylglyoxylic acids were both significantly elevated in the urine (Table 29). Levels of phenylglyoxylic acid were the most sensitive indicator when styrene concentrations were in the range of 1 to 20 ppm. On the other hand, urinary hippuric acid levels did not correlate with intensity of exposure at the concentrations of styrene vapor studied in this experiment. However, in a more recent investigation, Ikeda et al. (1974) noted that a significant increase in urinary hippuric acid levels was observed among workers exposed to styrene at concentrations of 50 to 200 ppm for 160 minutes. In this study, mandelic and phenylglyoxylic acid levels were maximally elevated two to five hours after termination of exposure (returning to normal after about 30 hours), whereas hippuric acid levels reached a peak several hours later (returning to normal after one to two days). The delayed appearance of hippuric acid is consistent with the observation that it is derived from mandelic acid. When styrene exposure was reduced to 4 to 60 ppm for 120 minutes, hippuric acid levels were not elevated in the urine, although urinary concentrations of mandelic and phenylglyoxylic acids were both enhanced. A comparison of the urinary

Table 29. Metabolite Levels in Urine of Workers Exposed to Styrene[a]

| No. of workers | Styrene concentrations (ppm) | Metabolites in urine (mg/liter) | | | Ratio $\frac{\text{mandelic acid}}{\text{Ph-glyoxylic acid}}$ |
|---|---|---|---|---|---|
| | | Hippuric acid | Phenylglyoxlic acid | Mandelic acid | |
| 6 | 10-30 | 438<br>(326-588) | 381<br>(298-487) | 875<br>(505-1515) | 2·3 |
| 4 | 7-20 | 556<br>(263-1175) | 287<br>(183-449) | 473<br>(319-702) | 1·7 |
| 4 | 1-20 | 494<br>(238-1022) | 201<br>(153-263) | 310<br>(189-518) | 1·5 |
| 7 | <1 | 309<br>(198-482) | 98<br>(46-213) | 137<br>(49-385) | 1·4 |
| 9 | 0 | 350<br>(199-616) | 19<br>(11-34) | 92<br>(47-178) | |

[a] Modified from Ohtsuji and Ikeda (1970)

half-lives of mandelic and phenylglyoxylic acids among male workers revealed values of 7.8 and 8.5 hours, respectively. Philippe and coworkers (1971) agreed that mandelic acid is more rapidly excreted than phenylglyoxylic acid, but noted that its biological half-life increases with styrene exposure intensity above 100 ppm. Thus, the measurement of urinary phenylglyoxylic acid and the determination of the mandelic acid/phenylglyoxylic acid ratio was suggested as a useful procedure for monitoring the degree of styrene exposure.

Quantitative correlates of styrene exposure with levels of urinary metabolites have been attempted by others in recent years. For this purpose, urinary levels of mandelic acid, expressed as mg/ℓ of urine or mg/g of creatinine, are correlated with air concentrations of styrene. It was reported (Harkonen et al., 1974) that urine samples taken at the end of an eight hour work shift contained 3000 mg mandelic acid per liter of urine when workers were exposed to a time-weighted average styrene exposure of 100 ppm. However, Gotell and coworkers (1972) determined that 1000 mg/ℓ of mandelic acid in urine corresponded to a time-weighted average styrene exposure of 50 ppm, and 2000 mg/ℓ corresponded to an exposure of 100 ppm of styrene. Moreover, these investigators found that in a group of workers exposed to concentrations of styrene greater than 150 ppm, a strongly negative correlation was obtained between styrene exposure and urinary levels of mandelic and phenylglyoxylic acids.

More recently, these surprising results were clarified by Engstrom and coworkers (1976) who found that the half-time of elimination of mandelic acid decreased as exposure levels of styrene increased from 23 to 248 ppm. In addition, a biphasic elimination rate was observed for mandelic acid, showing a rapid phase from 0 to 18 hours post-exposure and a slow phase from 19 to 64 hours post-exposure. Since dose-dependent elimination of xenobiotics is a commonly observed phenomenon, it may reasonably be speculated that enhanced detoxification mechanisms (i.e., enzyme induction) may result from high-level styrene exposures (see Section III-B-7). As a biological monitoring tool, levels of mandelic acid in urine taken at the end of a work shift correlated highly (r = 0.93) with the eight-hour time-weighted average concentration of styrene in ambient air.

It is not presently possible to resolve the apparent inconsistencies reported in mandelic acid excretion rates at levels of styrene greater than 150 ppm. Whereas Engstrom and coworkers (1976) reported that the excretion rate of mandelic acid increases with styrene dose, Philippe et al. (1971) and Gotell et al. (1972) found that the rate decreases. Consequently, any program of biological monitoring for exposure to styrene will probably require the concommitant analysis of styrene levels in air in order to adequately define the potential exposure.

Analytical methods for the detection of mandelic and phenylglyoxylic acids in urine are well-validated. Major reliance is placed on gas chromatographic determination of the derivatized metabolites subsequent to their extraction from urine (Buchet et al., 1974; Bauer and Guillemin, 1976; Lhoest et al., 1976; Engstrom and Rantanen, 1974). The inclusion of a preliminary paper chromatographic separation of urine prior to gas chromatographic analysis was reported to increase the sensitivity of the mandelic acid assay by a factor of ten (Slob, 1973). Additional methods of analysis include colorimetric techniques (Ohtsuji and Ikeda, 1970) and a new isotachophoretic procedure which also identifies hippuric acid (Sollenberg and Baldesten, 1977).

In an attempt to define the body burden of styrene and ethylbenzene among 25 polymerization workers, Wolff and coworkers (1977) analyzed subcutaneous fat samples taken at various times after exposure. All 15 styrene workers who had been removed from work for less than three days had detectable levels of styrene in the fat. On the other hand, removal from exposure for more than three days was associated with an absence of styrene in the subcutaneous fat. These analyses also revealed the presence of ethylbenzene in 21 of the 25 workers, thereby indicating a greater persistence in the body, possibly due to its less efficient metabolism. Thus, it was concluded that although styrene rapidly disappears from the urine and breath, indirect exposure may still occur for several days to styrene which has been sequestered in body fat stores. This principle is applicable to ethylbenzene as well, since it apparently persists in the fat for even longer periods.

In a later study this same group (Wolff et al., 1978) monitored urinary levels of mandelic and phenylglyoxylic acids, and blood levels of styrene in 491 styrene polymerization workers. Styrene levels in subcutaneous fat samples were determined in 25 workers. The limit of detection for styrene in fat was .2 ppm., while for urinary metabolites it was approximately 10 mg/l. Blood levels of styrene were determined below 1 ppb. Workers were divided into groups exposed to higher than 5 ppm. styrene levels (peak levels of 8-30 ppm), 1-5 ppm. levels, and less than 1 ppm. styrene levels. In a group examined within four hours of last exposure, the highest frequency of elevated urinary metabolites and blood styrene concentration was found in those workers exposed to more than 5 ppm levels (40-60%). Workers who had elevated test values showed a correlation between urinary metabolites, blood styrene concentration, and styrene in fat. However, in the overall population studies, urinary metabolites were undetectable in the majority of workers (341/477) and the correlation between blood and urinary determinations was poor. The authors suggest that this may be due to the different elimination kinetics of styrene in blood, and of urinary mandelic and phenylglyoxylic acids, respectively. These studies confirm that urinary and blood levels decrease rapidly as time from last exposure lengthens, and that styrene levels in fat are the most prolonged values that were measured.

Uptake and retention of styrene was determined in three workers employed in a Swedish polymerization plant (Engstrom et al., 1978). The concentration of styrene in ambient air was monitored continuously during the work week in all breathing zones. Total uptake was estimated based on time weighted inspiratory air concentrations, and adipose concentrations were determined from subcutaneous fat samples. Measurements indicated that the time weighted inspiratory air level of styrene was 7.5-20 ppm. The mean daily styrene uptake varied from 193-558 mg. Variations in styrene levels measured in adipose tissue were observed during the work week. Monday morning adipose levels of 2.8-8.1 mg/kg were recorded, while Friday afternoon measurements were 4.7-11.6 mg/kg. The authors indicate that in all three workers a moderate increase (3-7%) in adipose styrene content was seen during the work week. Longer duration studies are needed to determine whether a cumulative effect is seen in the adipose tissue of workers constantly exposed to styrene.

Engstrom and coworkers (1978) monitored ambient air styrene levels in a reinforced plastics factory during a work day and determined urinary mandelic acid and hippuric acid content in 47 workers (9 females and 38 males) at the same facility. Measurements of air levels in different breathing zones were carried out for 30 minute intervals over the entire day. Urinary metabolites were assayed from samples collected at the end of the workday. The individual time weighted (8 hours) averages for different samples varied from 4 to 291 ppm, with a peak sample value of over 700 ppm. Urinary mandelic acid concentration correlated very well with the time weighted styrene air levels (coefficient=.93), while hippuric acid level fluctuations over the working day were irregular. Almost half of the workers (23/47) showed urinary mandelic acid levels that indicated 8 hour exposure to more than 55 ppm styrene.

Techniques to monitor for the absorption of compounds related to styrene and ethylbenzene (i.e., α-methylstyrene, divinyl benzene) are not readily available in the published literature. However, a Russian study (Aizvert, 1975) has indicated that the presence of atrolactic acid in the urine may be used as a test for exposure to α-methylstyrene. The authors reported that 26.2% of an inhaled dose of α-methylstyrene was excreted as urinary atrolactic acid during the five days following exposure.

### (2) Effects on Worker Health

Numerous adverse effects on health have been attributed to styrene exposure. In many cases, however, it is difficult to attribute specific clinical findings to styrene exposure alone. Moreover, it is not usually possible to define the extent of exposure which corresponds to particular toxic symptoms.

Reports from East-European countries and Russia have linked chronic occupational exposure to styrene with: menstrual disorders and toxemia of pregnancy (Zlobina _et_ _al_., 1975); decreased blood glucose and increased glucose tolerance (Chmielewski _et_ _al_., 1973); leukocytosis, erythrocytopenia, muscle-chronaxia changes, decreased coproporphyrin excretion, decreased blood cholinesterase activity, and histological changes in some organs at exposure levels of 1.2 and 11.7 ppm (Li, 1963); skin infections and neurasthenic syndrome at average exposures of 164 ppm or less for 1.8 years (Simko et al., 1966); headache, weariness, somnolence, and dyspeptic disorders at exposures of 47 to 94 ppm (Huzl et al., 1967); and increased urinary coproporphyrin excretion and elevated lactic acid dehydrogenase activity with exposures of 24 ppm (Klein and Zak, 1969). Further reports abstracted from the foreign literature have associated combined styrene-butadiene-ethylbenzene exposures with diseases of the nervous system and digestive organs (Abdullaeva, 1973); decreased peripheral vascular tonus and stability (Alekperov et al., 1970a; Vinokurova, 1970a); altered myocardial function (Alekperov et al., 1970b; Vinokurova, 1970b); alterations in blood content of cholesterol, lecithin, and lipoproteins at styrene exposure levels of 0.5 to 32 ppm (Lukoshkina, 1970; Lukoshkina and Alekperov, 1973); and alterations in gastric juice components and gastric mucosa function (Bashirov, 1975). Additional evidence concerning occupational exposure to α-methylsytrene (with or without exposure to butadiene) suggested neurological and reflex effects (Minaev, 1969; Ogleznev, 1963), liver dysfunction (Sergeta et al., 1975), cardiovascular disorders (Konstantinovskaya, 1972), and vitamin $B_{12}$ deficiency (Bravve, 1974).

Neurological symptoms in workers exposed to styrene in the plastics industry have been studied by Klimkova-Dentschova (1962) and Roth and Klimkova-Deutschova (1963). A group of 30 women and five men reporting to the clinic with varied symptoms of headache, fatigue, tremors, and neurasthemic symptoms were given neurological examinations. Average exposure time of the group was 1.9 years at levels from 20 ppm to 130 ppm styrene. EEG abnormalities were noted in 13/18 (72%) workers studied; these involved irregular alpha rhythms, alternating rapid activity and low amplitude patterns, and the presence of theta waves. Patterns indicating sleep or reduced vigilance were also noted. A high incidence (74-95%) of vegetative (autonomic) nervous system symptoms, peripheral, and extra-pyramidal neurological symptoms in these styrene workers was also reported. Exposure to other chemicals cannot be evaluated, and these studies deal with a selected population that has already shown subjective symptoms of toxicity.

Many years of industrial experience with styrene have established that symptoms of mucosal irritation and general discomfort are common complaints among exposed workers (Zielhuis et al., 1964). A summary of data regarding subjective symptoms resulting from chronic styrene exposure (average exposure below 100 ppm) is presented in Table 30. These data were thought to support the safety of a 100 ppm exposure limit with regard to serious or permanent health impairment (AGGIH, 1977).

On the other hand, examinations of biochemical functions among styrene workers have indicated certain metabolic disorders. Workers with exposure to styrene for an average period of ten years were found to have reduced blood platelet numbers with increased platelet adhesion, which was possibly related to disorders in lipid metabolism and thrombopoiesis (Chmielewski and Renke, 1976). In addition, workers with long-term styrene exposures displayed abnormalities in blood coagulation and fibrinolysis, which could be explained by an effect of styrene on the liver. Since workers with short-term (one year) styrene exposures were not affected, it was presumed that the toxic effects observed were a consequence of chronic exposure (exposure intensity not reported). Further studies (Chmielewski and Hac, 1976) on these same workers

Table 30. Subjective Symptoms Among Workers Processing Reinforced Polyesters[a]

| Symptoms | Group A n = 8 | Group B n = 8 | Group C n = 22 | Group D n = 6 | Controls n = 5 |
|---|---|---|---|---|---|
| physical fatigue | 4[b] | 5 | 2 | 1 | 2 |
| apathy | 4 | 4 | 3 | 1 | 0 |
| mental fatigue | 3 | 5 | 2 | 0 | 0 |
| epigastric oppression | 1 | 2 | 1 | 1 | 0 |
| gastric pain | 1 | 1 | 1 | 1 | 0 |
| sickness | 2 | 0 | 1 | 1 | 0 |
| hunger | 2 | 0 | 2 | 3 | 2 |
| anorexia | 4 | 2 | 1 | 3 | 0 |
| dizziness | 2 | 4 | 0 | 3 | 1 |
| headache | 4 | 2 | 3 | 2 | 2 |
| pressure round head | 4 | 5 | 2 | 1 | 1 |
| feeling groggy | 1 | 3 | 1 | 2 | 0 |
| hypersensitivity against alcohol | 1 | 1 | 2 | 1 | 0 |
| perspiration of the hands | 2 | 2 | 1 | 1 | 1 |
| general perspiration | 4 | 4 | 2 | 1 | 1 |
| palpitations | 1 | 1 | 0 | 0 | 1 |
| breathlessness | 1 | 2 | 1 | 0 | 2 |
| drowsiness | 5 | 5 | 4 | 3 | 0 |
| tearflow | 5 | 4 | 3 | 0 | 1 |
| irritation of eyes | 5 | 5 | 3 | 5 | 0 |
| sneezing and coughing | 4 | 2 | 2 | 4 | 1 |
| nervousness | 2 | 1 | 1 | 1 | 1 |
| elation | 1 | 0 | 0 | 1 | 0 |
| agitation | 2 | 2 | 1 | 0 | 1 |
| nervous tension | 3 | 2 | 3 | 0 | 1 |

---

[a] Modified from Zielhuis _et_ _al_., 1964

[b] 1 = in 0-20% of workers;
2 = in 21-40%;
3 = in 41-60%;
4 = in 61-80%;
5 = in 81-100%

revealed no deficiency in liver function in either group. However, workers with long-term styrene exposure exhibited a reduction in serum levels of alpha- and beta-lipoproteins and cholesterol. The possibility that chronic styrene exposure may alter patterns of steroid production by the adrenal glands or metabolism by the liver could not be statistically confirmed (Wink, 1972).

The health effects of exposure to styrene vapor in a German production and polymerization facility were investigated by Thiess and Friedheim (1978). Styrene levels in workroom air were generally less than 1 ppm, with no concentration exceeding 10 ppm. Clinical disease histories and hematology and blood chemistry examinations were carried out on 177 employees having exposure durations lasting from 1-38 years. Controls consisted of workers from another production facility which did not produce styrene monomer or polymer. The chemical exposure pattern of the control group was not specified. No significant abnormalities in either laboratory findings or case histories were observed. Urinary mandelic acid levels determined on these workers indicated that low exposure to styrene was present at these production facilities. Mortality studies of workers at this same facility indicated no increase in deaths from tumors.

An extensive clinical study of 494 styrene workers in the United States has confirmed many of the observations of earlier investigators (Lorimer et al., 1977). Symptoms associated with styrene exposure include prenarcotic symptoms (13% of the workers affected), mucous membrane irritation (18%), wheezing or tightness in the chest (11%), recurrent tracheo-bronchial irritation (7.6%), chronic bronchitis (18.7%), and airway obstruction defined as FEV/FVC < 75% (35.3%). In general, workers with the highest styrene exposure experienced the highest prevalence of symptoms.

Further work (Lorimer and coworkers, 1978) has analyzed the results of this extensive health survey covering 493 production workers at a facility manufacturing styrene and processing polystyrene. Comparisons were made and statistically analyzed between workers classified into either high or low exposure categories. This distinction was made on the basis of work history, spot testing for urinary styrene metabolites, and some limited air sampling data obtained through NIOSH and the production company. Groups were subdivided into three sections based on duration of exposure to styrene. Statistically significant differences between high and low exposure groups were noted in several categories. These included acute symptoms such as lightheadedness, dizziness, and headache, and lower respiratory symptoms such as coughing and wheezing. Relative lymphocytosis was seen to increase in the high exposure group as the duration of exposure in this group increased. Large pulmonary airway obstruction was increased in workers showing detectable urinary mandelic acid when compared to workers in whom this urinary metabolite could not be detected. Liver gamma-glutamyl transpeptidase levels were elevated more frequently in the high styrene exposure group (1.7% vs. 7.2%). Lowered nerve conduction velocities were recorded in the high exposure workers (∿16% of those tested). Lymphocyte karotyping was carried out on a small number of individuals (5 test, 2 control). Two of the test subjects had a high number of chromosome gaps and breaks; these two had the longest incidence of high styrene exposure (>20 yrs.) in the test group. Interpretation of these findings is complicated by several factors. For over one half the period covered by this study (1943-1963), this facility used benzene in production, and thus long term employees were exposed to an agent which produces well documented liver and hematological effects. The karotyping results were successful in too few of the subjects tested to draw any inferences concerning chromosome breaks.

Among the more significant recent findings concerning occupational exposure to styrene are reports of its effects at low levels on mental functions. Workers were examined who had long-term exposure (mean 4.9 years) to styrene at low levels (urinary mandelic acid levels less than 674 mg/ℓ, corresponding to an 8 hour TWA exposure of 2.5 ppm) and at higher levels [mandelic acid levels more than 1,762 mg/ℓ, corresponding to an 8 hour TWA exposure of 75 ppm] (Lindstrom et al., 1976). Although the comparison between exposed and non-exposed workers showed few statistically significant differences in psychological functions (visual inaccuracy and a high level of inhibition in personality tests), comparisons between low and high exposure groups of workers revealed greater differences. Visuomotor inaccuracy and poor psychomotor performance were significantly related to high mandelic acid concentrations in the urine. Moreover, mildly abnormal electroencephalograms (EEG's) were found in 23 out of 96 styrene-exposed workers (24%), which corresponded to higher mean mandelic acid concentrations than in workers with normal EEG's (Seppalainen and Harkonen, 1976). Symptoms of peripheral nerve dysfunction, as measured by nerve conduction velocity, were inconsistent and not indicative of an exposure-related trend. However, Savolainen (1977) has recently reported that styrene and styrene oxide undergo limited binding to central nervous system macromolecules and can elicit weak neurotoxic (encephalopathy and neuropathy) effects.

Harkonen and coworkers (1978) have examined neurophysiological and psychological effects in 98 male workers exposed to styrene in 24 reinforced plastic facilities. Workers were placed into one of four groups based on their urinary mandelic acid concentrations. An increase of abnormal electroencephalograms (from 10% to 30%) was seen when subject groups showing <700 mg/ℓ mandelic acid were compared. Visuometer accuracy showed impairment at mandelic acid levels of >800 mg/ℓ, and psychometer performance was affected when mandelic acid levels exceeded 1,200 mg/ℓ. Intellectual performance was not found to have changed after work in styrene facilities, as measured by standard intelligence testing. The authors indicate that these effects are seen at levels of exposure that correspond to an 8 hour time weighted average of 55 ppm or less.

Neurophysiological testing of thirty three styrene workers has also been described by Rosen and coworkers (1978). Three groups of workers exposed to styrene during different manufacturing or production processes were compared to 17 patients showing neurological disorders from mixed solvent exposure and a control group without solvent exposure. The ten styrene workers who showed symptoms of neuropathy, similar to the symptoms observed in the mixed solvent group, were from the group exposed to the highest levels of styrene. This was in a polyester boat facility where 1974 measurements indicated a mean level of 125 ppm styrene. Earlier conditions at this facility indicate that higher levels of exposure were likely. The observed neurological changes included altered sensory nerve (median, ulmar) action potential, some decreased sensory nerve conduction velocity, diffuse slow EEG activity, and central and fronto-central fast EEG activity. The diffuse slow pattern incidence did not correlate with styrene exposure intensity. The authors conclude that EEG changes were either too small or too non-specific to aid in styrene exposure diagnosis, while sensory nerve measurements appear to show good sensitivity to styrene effects.

Neurological studies were carried out on six volunteers (3 styrene workers, 3 normal subjects) who were exposed to styrene vapor at 50-300 ppm for ninety minutes (Oltramare et al., 1974). At exposure levels of 100 ppm and 200 ppm, the three styrene workers showed decreased performance in tests of reaction times to visual stimuli and visual-acoustic stimuli (compared to results from pre-exposure testing). Since this work was carried out on only three subjects, further experimentation is needed to confirm the results noted.

Concern over the leukemogenic and clastogenic effects of benzene have prompted a closer examination of structurally related compounds for their ability to induce chromosome damage in somatic cells. Thus, it has now been demonstrated that among workers chronically exposed to styrene an increased incidence of chromosomal aberrations occurs in cultures of their blood lymphocytes (Meretoja _et_ _al_., 1977). Ten styrene-exposed workers and five unexposed controls were used for the study. Absorption of styrene was confirmed by the presence of mandelic acid in the urine, although an accurate estimate of total exposure could not be made. The incidence of chromosome abnormalities (primarily chromosome-type breaks) ranged from 11 to 26% in the cells of styrene-exposed workers, as compared to three percent or less in the control group. The possibility that these workers may also have been exposed to other chemicals, either on the job or at home, could not be completely eliminated. Nevertheless, since exposure to styrene was confirmed by metabolite identification, a causal relationship was strongly implied.

A follow up study on these same subjects was carried out one year later (Meretoja _et_ _al_., 1978). Urinary mandelic acid levels in 9/10 workers studied were lower than those observed one year earlier. The frequency of abnormal lymphocytes (both stable and unstable changes) in styrene workers varied from 10-26%, while controls showed a 1-4% frequency. The authors conclude that both the pattern and frequency of lymphocyte aberrations has remained the same over the one year period. This incidence of aberrations is higher than that reported for either benzene or vinyl chloride workers.

Flieg and Thiess (1978) have carried out similar studies on lymphocyte aberrations in workers exposed to styrene in different types of manufacturing facilities. Workers in styrene manufacturing plants and polystyrene manufacturing plants showed low urinary mandelic acid levels and no increase in chromosome aberrations over controls. Workers exposed to styrene in a plant processing unsaturated polyester resins had elevated urinary mandelic acid levels and showed an increase in the frequency of aberrant lymphocytes. Both inclusive and exclusive gaps were increased over controls. In 14 workers the range in frequency of inclusive chromosome gaps was 4-20%, while the mean in twenty controls was 5.5%. Ten of the fourteen workers showed a higher percentage of inclusive gaps than the control mean. The authors comment that workers in this last facility came in contact with various solvents during their work. The use of peroxides in the curing process will generate styrene oxide in the working area atmosphere and this chemical could be the agent responsible for the lymphocyte effects seen (based on its capability to induce mutations during in vitro tests).

Hematological investigations on nine workers exposed to styrene vapors have been carried out by Oltramare and coworkers (1974). Four workers, involved in three different types of manufacturing operations using styrene resins, showed lymphocytosis (38-47% lymphocytes in peripheral blood). Exposure ranges for the different facilities were estimated at 10-35 ppm styrene, 12-82 ppm, and 10-560 ppm.

b. Epidemiologic Studies

Serious concern has recently arisen over the health hazards of styrene as a result of reports showing an excess incidence of leukemia among workers in the styrene-butadiene rubber industry. It was first reported in 1976 that a six-fold excess of leukemia and lymphoma was found among workers at a styrene-butadiene plant (McMichael et al., 1976). Subsequent to that report, a briefing on styrene-butadiene was called by the National Institute for Occupational Safety and Health on April 30, 1976, to review the hazards of styrene-butadiene production and to gather additional information (National Institute for Occupational Safety and Health, 1977). Reports of an excess of deaths attributable to leukemia and lymphoma at several plants in the United States were presented. A study of nine leukemia cases found in two styrene-butadiene rubber production plants in Port Neches, Texas indicates that these workers had a long duration of potential exposure (range of exployment = 17-28 years) (Meinhardt et al., 1978).

Mortality data on 560 styrene-polystyrene polymerization workers at one plant has been reviewed by Nicholson and coworkers (1978). This group, representing five years or more of work experience, did not show an increased frequency of death from cancer. However, review of an additional 444 death certificates of employees with six months or more of work experience at this plant showed twelve deaths resultant from leukemia or lymphoma. Since the death certificates were randomly collected, the authors state that further analysis should be conducted before conclusions can be drawn.

The lack of detailed information concerning simultaneous exposure to chemicals other than styrene (e.g., benzene) and the need for more extensive epidemiologic studies precludes a definitive judgement at this time. In addition, it has been reported (Frentzel-Beyme et al., 1978) that in a study of West German polystyrene workers there was no evidence of an excessive incidence of leukemia. However, the lack of leukemia cases may be due to extremely low styrene exposures (currently less than 1 ppm). Urinary mandelic acid levels in 61/67 workers tested at this facility were less than 50 mg/ℓ.

### c. Controlled Metabolic Studies in Humans

#### (1) Absorption and Excretion

The uptake of various solvents, including styrene and ethylbenzene, has been determined from studies where exposure has occurred by inhalation or direct contact with the skin. Astrand and coworkers (1974) performed a detailed investigation of the uptake and elimination of styrene in human volunteers exposed to concentrations of 50 and 150 ppm styrene in air. The absorption of styrene across the alveolar membranes and into arterial blood was found to be extremely rapid, indicating high solubility of styrene in the blood. Increased ventilation, as produced by light work, markedly increased the absorption of styrene because the blood is exposed to greater amounts of solvent-containing air. Thus, when alveolar ventilation was tripled by light exercise, the concentration of styrene in arterial blood was tripled, whereas the alveolar concentration of styrene increased only slightly. Therefore, measurement of the concentration of styrene in alveolar air provides a poor index of the extent of absorption. Ranking various solvents according to their percentage of uptake based on blood and tissue solubility produced the following results (largest uptake first): styrene, aromatic components of white spirit, toluene, trichloroethylene, aliphatic components of white spirit, methylene chloride, and methylchloroform (Astrand, 1975).

Styrene can be detected in alveolar air up to 24 hours after termination of exposure (30 minutes) at 50 or 150 ppm (Astrand *et al.*, 1974). Stewart and coworkers (1968) have noted that styrene excretion from the lung is rapid and exponential, but dependent on the concentration and duration of exposure. It was calculated that 1.2% of an absorbed dose of styrene (117 ppm x 2 hours) was excreted via the lungs within the first four hours after exposure. By comparison, Astrand and coworkers (1974) determined that 50% of an absorbed dose (50 ppm x 30 minutes) of styrene was excreted in the urine as mandelic acid. Others (Bardodej and Bardodejova, 1970) reported that 64% and 85% of the absorbed doses of inhaled ethylbenzene and styrene, respectively, were excreted as urinary mandelic acid (Table 31). These investigators, however, were unable to detect large amounts of unchanged styrene or ethylbenzene in expired air following eight hours of inhalation exposure. It was suggested (Astrand _et al_., 1974) that failure to correct for background levels of mandelic acid excretion and the low concentrations employed (22 ppm styrene) may account for the discrepancies.

Pulmonary absorption and excretion of styrene was determined in six volunteers by Fernancez and Caperos (1977). Styrene exposure varied from 70-200 ppm for periods of 4-8 hours. Pulmonary absorption studies indicated a retention of 81.8-92.7% of styrene administered at various concentrations. Alveolar pulmonary concentrations of styrene declined rapidly within one hour after the termination of exposure at all levels. The proportion of styrene eliminated by the lungs was only 2.6% of the total absorbed dose. Since blood levels of styrene decline rapidly following exposure, metabolism and urinary excretion play the major role in elimination.

Fiserova-Bergerova and Teisinger (1965) have conducted similar studies of pulmonary retention of styrene vapor in seven volunteers exposed to concentrations of 15-38 ppm levels. Exposure periods were for five hours. Styrene retention was from 47-73% following inspiration and did not change during the exposure period. Alveolar air contained about 6% of the inspired styrene. Elimination of styrene from alveolar air showed half lives of 1.7 minutes and 7.6 minutes thus indicating a two compartment elimination model. After the termination of exposure styrene could not be detected in exhaled breath.

Table 31. Retention, Biotransformation, and Elimination of Ethylbenzene and Styrene and Their Metabolites in Man[a]

| | Ethylbenzene | Styrene |
|---|---|---|
| Concentration of vapor in the inspired air (ppm) | 23; 43<br>46; 85 | 22 |
| Duration of inhalation (hours) | 8 | 8 |
| Percentage[b] of vapor retained in the respiratory tract | 64 | 61 |
| Excreted in expired air in unchanged form after inhalation was terminated | Traces | 0[c] |
| Percentage[b] of retained dose eliminated as: | | |
| Mandelic acid | 64 | 85 |
| Phenylglyoxylic acid | 25 | 10 |
| Methylphenylcarbinol | 5 | 0 |
| Acetophenone | Not demonstrated[c] | |
| Styrene oxide | | |
| Phenylethyleneglycol | | |
| ω-Hydroxyacetophenone | | |
| Hippuric acid | Elevation not demonstrated[c] | |
| Mercapturic acid | | |

---

[a] Bardodej and Bardodejova, 1970

[b] Arithmetic averages of eighteen experiments with ethylbenzene, thirteen with styrene

[c] By the methods used (e.g., less than 2%).

Experiments on the uptake and elimination of styrene following inhalation exposure of seven volunteers has been reported by Engstrom and co-workers (1978). Subjects were exposed to 50 ppm styrene at rest for 30 minutes, given a twenty minute recovery, and then exposed for three consecutive 30 minute periods with increasing work on a bicycle. The mean retention under conditions of rest or work was 63% of the inspired styrene. During the last 30 minute work period, total styrene taken up was 5-6 times greater than during the initial rest period, indicating greater ventiliation rate effects. Elimination of styrene by the airways during 19 hours after exposure was about 3% of the total styrene retained. Adipose tissue samples retained measurable styrene for as long as thirteen days following exposure. The estimated half life of styrene in adipose tissue was from 2-4 days. The estimated percentage of styrene sequestered in adipose tissue was 8% of the total retained styrene. However, this value will be effected by the size of the total body fat depot. The authors state that since adipose tissue shows a slow elimination rate the risk of styrene accumulation in workers may be present.

Ramsey and Young (1978) studied the pharmacokinetics of inhaled styrene in four volunteers exposed to 80 ppm for six hours. Blood levels of styrene were shown to decline rapidly after exposure was terminated, with half lives calculated at 16 hours and 13 hours for the two compartments of the model constructed (blood=1st compartment, fat=2nd compartment). Based on this model and the derived values, the authors conclude that no long term accumulation of styrene will occur in workers exposed to 80 ppm styrene over a five day work week. This conclusion is not in accord with those of Engstrom (1978) and reflects several differences in the two studies. Static exposure was used in the Ramsey study, and body fat was assumed to constitute 10% of the body weight. In the

Engstrom study the derived half life of styrene in adipose tissue was considerably longer than the value applied to the second compartment of the Ramsey model.

Correlation of urinary mandelic acid and phenylglyoxylic acid levels with controlled styrene exposures has been reported by Guillemin and Bauer (1978). Nine subjects were exposed to styrene vapor at 40 to 200 ppm for four to eight hours. Rate constants for elimination of these two metabolites were not effected by level or duration of exposure. The best correlation of metabolite levels with styrene exposure (.91) was obtained when the sum of both metabolites was cummulated over four days of measurements. For samples taken at a single time point, either mandelic acid measured at the end of the work shift, or the sum of mandelic acid and phenylglyoxylic acid measured on the morning after the last exposure, gave relatively poor correlations (.71 or .77).

Exposure of the skin to ethylbenzene or styrene leads to significant absorption (Dutkiewicz and Tyras, 1967; 1968). The rate of skin absorption for ethylbenzene and styrene was considerably greater than for other common solvents (Table 32). In addition, it was shown that the amount of absorbed styrene or ethylbenzene excreted as urinary mandelic acid was much less when exposure occurred by the skin as opposed to inhalation. These results indicate that the metabolic disposition of these compounds may be dependent upon the route of exposure.

The percutaneous absorption of styrene vapors in ten human volunteers has been studied by Riihimaki and Pfaffli (1978). Subjects were exposed to 600 ppm styrene for 3 1/2 hours, during which time three ten minute work intervals were included. Full face respirators provided inhalation protection. Blood levels of styrene reached a plateau in three hours (during exposure), and then declined rapidly in the next four hours after the termination of treatment. The

Table 32. Skin Absorption of Styrene and Ethylbenzene[a]

| Substance | Rate of Absorption ($mg/cm^2/hr$) | 24 Hour Mandelic Acid Excretion (% of absorbed dose) |
|---|---|---|
| Ethylbenzene | 22-33 | |
| Ethylbenzene from aqueous solutions (112-156 mg/ℓ) | 0.11-0.21 | 4.6 |
| Styrene | 9-15 | |
| Styrene from aqueous solutions (66.5-269 mg/ℓ) | .040-.180 | 13 |
| Aniline | 0.2-0.7 | |
| Benzene | 0.4 | |
| Nitrobenzene | 0.2-3.0 | |
| Carbon Disulfide | 9.7 | |

[a] Data from Dutkiewicz and Tyras, 1967;1968.

blood levels of styrene observed were comparable to those seen following inhalation exposure to ~20 ppm styrene. The authors estimated that percutaneous absorption of this level of vapor is ten times more effective than with the pure liquid compound.

### (2) Physiologic Effects

The dose-related physiologic effects of acute styrene exposure in humans have been studied using controlled inhalation experiments. When five volunteers were exposed for one to seven hours to styrene at 50, 100, 200, and 375 ppm, adverse effects were noted only at the highest concentration (Stewart et al., 1968). Symptoms related to the exposure included mild eye irritation within 15 minutes and impairment of neurological function (manual dexterity; coordination) within one hour. In a similar study, Gamberale and Hultengren (1974) found that inhalation of styrene at 350 ppm caused a significant impairment in tests of reaction time. However, no performance decrements in tests of perceptual speed or manual dexterity were noted at this concentration. With acute exposures below 350 ppm, styrene apparently had no effect on psychological or neuromuscular functions. Nevertheless, it should be noted that duration of exposure, rather than intensity, may have an important bearing on the physiologic actions produced by styrene, since arterial blood concentration continued to increase throughout the two-hour exposure period.

Earlier studies have established that high level styrene exposure (800 ppm for four hours) to human volunteers was associated with impaired psychomotor responses during tapping rate and steadiness tests (Carpenter et al., 1944). In addition, styrene at the 800 ppm level produced immediate eye and throat irritation, increased nasal mucus secretion, and subjective symptoms of drowsiness, weakness, unsteadiness, and lingering metallic taste.

Controlled human studies involving exposure to ethylbenzene or α-methylstyrene which detail the physiologic effects of exposure have not been encountered.

### d. Poisoning Incidents

Reported cases of accidental styrene poisoning are relatively rare. However, from the limited data which are available, a possible relationship is suggested between acute styrene intoxication and transient visual impairment.

It was first reported in 1964 that a man working in the fiberglass industry and having repeated exposure to styrene developed a sudden and painless deterioration of vision (Pratt-Johnson, 1964). A general medical and neurological examination revealed no abnormalities other than a presumed bilateral toxic retrobulbar neuritis caused by styrene exposure. The patient's vision slowly returned to normal (20/20) after seven months, with complete recovery of visual acuity and visual fields within a year. In a more recent report of accidental styrene poisoning, Schwarzmann and Kutscha (1971) described the case of a student who developed blind spots in the centers of his eyes within a half-hour of spilling styrene on his left hand. Vision improved within one and one-half hours of the exposure, although the patient continued to suffer from an intense headache, numbness, hot and cold spells, and shakiness. Recovery was apparently complete within twelve hours after the initial exposure.

Published reports have not been encountered which describe incidents of poisoning by ethylbenzene, α-methylstyrene, or divinylbenzene.

## 2. Effects on Non-Human Mammals

### a. Absorption/Excretion Studies

Early experiments demonstrated that styrene is rapidly distributed in mammalian tissues and quickly eliminated from the body (Danishefsky and Willhite, 1954). Although the results were limited by the availability of sensitive analytical techniques, it was nevertheless shown that $\beta$-$^{14}C$-styrene is widely and maximally distributed to all major tissues within one hour of subcutaneous injection in the rat. Within 24 hours, 85% of the administered radioactivity was excreted; principally via the urine (71%) but also in the feces (<3%) and as respired $CO_2$ (12%). Almost three percent of the administered dose was recovered within 24 hours as unchanged styrene exhaled from the lungs.

More recent studies (Sauerhoff et al., 1976; Sauerhoff and Braun, 1976) confirm, for the most part, the observations of earlier investigators regarding styrene disposition. The oral administration of ring-labelled $^{14}C$-styrene to rats of both sexes at doses of 50 and 500 mg/kg resulted in excretion of more than 90% of the radioactivity in urine after 72 hours (Table 33). Elimination of radioactivity from body tissues was complete within 72 hours.

The kinetics of urinary metabolite elimination in rats following lip administration of 900 mg/kg styrene has been reported by Ogata and Sugihara (1978). Urine samples were separated using liquid chromatography and analyzed for mandelic acid, phenylglyoxylic acid, and hippuric acid content. The levels of all three metabolites peaked at 24 hours and then progressively declined.

A greater percentage of styrene excreted unchanged from the lungs of rats treated at 500 mg/kg was indicative of saturation of metabolic

Table 33. Percent of Administered $^{14}C$ Activity Recovered in 72 Hours Following a Single Oral Dose of 50 or 500 mg/kg $^{14}C$-Styrene[d]

| | 50 mg/kg[a] | 500 mg/kg[a] |
|---|---|---|
| Urine | 94.6 ± 1.9 | 90.3 ± 6.4 |
| Feces | 3.7 ± 1.3 | 1.5 ± 0.6 |
| Expired Air[b] | 1.3 ± 0.5 | 8.9 ± 4.4 |
| Tissues and Carcass[c] | - | - |
| Cage Wash | 0.4 ± 0.1 | 0.9 ± 0.4 |
| Recovery | 100.2 ± 1.3 | 98.7 ± 6.1 |

[a] Values are mean ± S. D. of 2 male and 2 female rats.

[b] Values for $^{14}C$ activity in expired air represent expired styrene.

[c] No detectable $^{14}C$ activity found in tissues or carcass.

[d] Sauerhoff *et al*., 1976.

pathways for styrene biotransformation (Sauerhoff et al., 1976). Moreover, urinary excretion of styrene at 50 mg/kg was biphasic (half-life values of 1.29 ± 0.19 and 8.13 ± 1.22 hours), whereas at 500 mg/kg excretion was monophasic (half-life value of 6.74 ± 0.67 hours). Sex differences in the excretion of styrene in expired air, with males excreting about twice as much styrene as females at both dose levels, probably resulted from the sequestering of styrene in females due to their greater fat deposits.

Results obtained with rats following an inhalation exposure to $^{14}C$-styrene at either 60 or 600 ppm for six hours generally confirmed the results of oral exposure studies (Sauerhoff and Braun, 1976). In this case, however, elimination of radioactivity in the urine was biphasic at both exposure levels. Half-life values for excretion (terminal phase) were 14.9 ± 6.5 hours and 19.2 ± 3.7 hours at exposures of 60 and 600 ppm $^{14}C$-styrene, respectively. Sauerhoff and Braun (1976) cited additional evidence which demonstrated that a disproportionate increase in blood levels of styrene results from increasing inhalation exposures (i.e., a twenty-five fold increase in blood levels with a twelve-fold increase in styrene concentration). This observation suggests a saturation of biotransformation mechanisms with increasing intensity and/or duration of exposure. It was further observed that the half-life value for styrene elimination increased from 24.5 minutes to 44.8 minutes when exposures were increased from 45 ppm (5 hours) to 520 ppm (5 hours). Thus, it is possible that greater amounts of styrene are deposited in body fat when excretion mechanisms are saturated.

The toxicologic significance of styrene at exposure levels where saturation of biotransformation mechanisms occur is not clear. However, by analogy to other aromatic toxicants (Gillette et al., 1974), it can be shown that a disproportionate accumulation of bioactivated toxic intermediates may occur when excretion mechanisms are overloaded. In the case of styrene, one can speculate that an abnormal accumulation of the reactive intermediate styrene oxide may accompany inhalation exposures in rats which exceed 600 ppm or oral exposures of 500 mg/kg. Nonetheless, data are not available to confirm this hypothesis.

The pharmacokinetics of styrene uptake in the rat following intravenous and inhalation administration has been described by Withey (1978). A two compartment model was used to evaluate the biexponential elimination curves determined for blood and several organs (heart, brain, liver, spleen, and kidney). These curves indicated that distribution of styrene to organs occurred rapidly and that elimination kinetics were similar for each organ. The time to reach blood saturation levels increased as the inhalation exposure levels of styrene (44.8 to 2,417 ppm) increased. The apparant volume of distribution calculated for this model (230 ml) was about ten times the blood volume and indicated extensive distribution to organs outside the blood compartment. Brain, kidney, and spleen showed higher levels of styrene than peripheral blood after varied inhalation exposures to styrene (470 to 2144 ppm), and perirenal fat showed the highest levels observed at eight to ten times the level found in other organs, confirming the high lipid solubility of styrene. Elimination of styrene following inhalation exposure at 2,417 ppm indicated blood half lives of 5 minutes and 320 minutes for the compound disappearance rates, while organ half life values were approximately five minutes and 35 minutes respectively.

Accumulation of styrene in rat brain and perinephric fat following 2-11 week exposures of rats to 300 ppm vapor was studied by Savolainen and Pfaffli (1977). Peak levels in both tissues were observed in 4 weeks, after which levels declined progressively with time. Perinephric fat styrene content was 40-70 times higher than brain content. The authors believe that adaption takes place involving metabolizing enzyme induction.

Teramoto and coworkers (1978) have examined the distribution of styrene in the tissues of rats exposed to 700 ppm styrene for four hour intervals. Concentrations of styrene for the following tissues were measured: adipose tissue, liver, brain, kidney, blood, spleen, and muscle. Levels measured were highest for adipose tissue and lowest for muscle. All tissues showed a similar biological half life of ∿2 hours, except for adipose tissue which was longer (levels detectable after 20 hours). Further investigations by this group (Teramoto, 1978) indicated that multiple exposures (5 x 4 hours) to 700 ppm styrene produced tissue distribution and elimination of compound similar to that observed after a single exposure. Repeated intraperitoneal administration of styrene (5 doses separated by 6 hr. intervals) at 350 mg produced a trend of increasing styrene concentration in adipose tissue.

The concentration of styrene in the principal organs of rats and mice has been studied following inhalation and dermal exposures (Shugaev and Yaroslavl, 1969). Table 34 shows that exposure of rats to an $LC_{50}$ dose (11.8 mg/ℓ) for four hours produced the greatest concentration of styrene in the perinephric fat. Absorption of styrene through the skin (tail) of rats also caused accumulation of significant quantities of the chemical in the brain and liver. These values were 50 to 70 percent of the concentrations found after inhalation exposure.

Mice exposed to lethal vapor concentrations (21.0 mg/ℓ ≈4930 ppm) of styrene accumulated the compound in the brain at a mean level of 18.02 milligram percent. This tissue concentration was nearly the same as in rats similarly exposed at lethal levels (Shugaev and Yaroslavl, 1969).

Table 34. Styrene Content in Rat Organs Following Inhalation and Dermal Exposures[a]

| Route of Administration | Duration and Concentration | Styrene Content in Rat Organs[b] | | | | |
|---|---|---|---|---|---|---|
| | | Brain | Liver | Kidney | Spleen | Perinephric fat |
| Inhalation | 11.8 mg/ℓ for four hours | 25.0<br>(17.7-32.4 ) | 20.0<br>(12.7-27.3) | 14.7<br>(2.8-26.7) | 19.1<br>(11.1-27.1) | 132.8<br>(109.9-155.7) |
| Dermal (tail immersion) | undiluted styrene for one hour | 14.2<br>(11.1-17.3) | 14.7<br>(10.7-18.7) | -- | -- | -- |

[a] Data from Shugaev and Yaroslavl, 1969.

[b] Milligram percent; mean concentration with confidence limits computed at $p = 0.05$.

### b. Metabolism and Pharmacology

The metabolic fate of styrene in laboratory mammals has been carefully investigated by numerous researchers for more than thirty years. It was originally reported (Spencer et al., 1942) that in rabbits and rats styrene is oxidized to benzoic acid, indicating cleavage at the vinyl double bond. Later, it was shown that styrene is quickly metabolized and predominantly excreted via the urine, probably in conjugated form (Danishefsky and Willhite, 1954; Smith et al., 1954).

The proposed metabolic pathways of styrene biotransformation in mammals are presented in Figure 12. It should be noted that the amounts of particular styrene metabolites produced (e.g., hippuric acid) will vary from rodents to man (Leibman, 1975).

Among the various metabolites to be identified in the biotransformation of styrene *in vivo* were phenylethylene glycol (El Masri et al., 1958), hydroxyphenethylmercapturic acid (James and White, 1967), hippuric acid (Spencer et al., 1942), 1- and 2-phenylethanol, vinylphenol (Bakke and Scheline, 1970), mandelic acid, and phenylglyoxylic acid (Ohtsuji and Ikeda, 1971). The major urinary metabolites of styrene following either oral or inhalation exposure in rats are mandelic, phenylglyoxylic, hippuric, and benzoic acids (Sauerhoff et al., 1976; Sauerhoff and Braun, 1976). The relative percentages of the various metabolites formed were found to be dose- and sex-related, however.

Further characterization of styrene metabolites formed after i.p. injection of $^{14}C$ styrene (label at the 8 position) into male rats was reported by Pantarotto et al., (1978). Ethyl acetate extracts of urine treated with trimethylanilinium hydroxide were analyzed using gas chromatography. Several

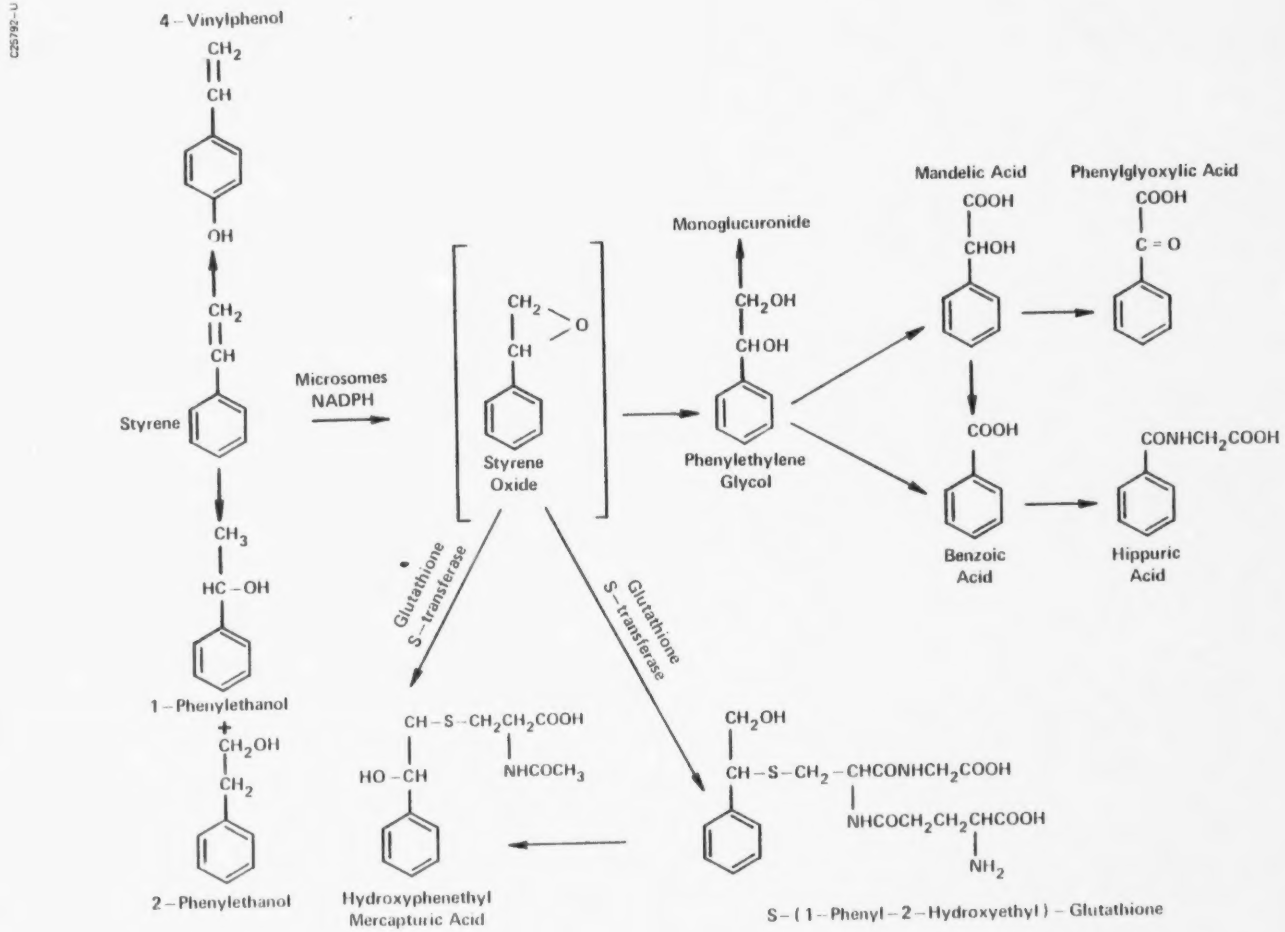

C25792-U
4-Vinylphenol
Styrene
Microsomes
NADPH
Styrene
Oxide
Monoglucuronide
Phenylethylene
Glycol
Mandelic Acid
Phenylglyoxylic Acid
Benzoic
Acid
Hippuric
Acid
Glutathione
S-transferase
Glutathione
S-transferase
1-Phenylethanol
2-Phenylethanol
Hydroxyphenethyl
Mercapturic Acid
S-(1-Phenyl-2-Hydroxyethyl)-Glutathione

Figure 12. Possible Pathways for Metabolism of Styrene in Mammals

unknown peaks were isolated by thin layer chromatography and characterized with mass spectrometry as containing phenolic derivatives of hippuric acid, mandelic acid, benzoic acid, and styrene. The authors postulated the formation of short lived styrene 3,4-epoxide and other unstable arene oxides as precursors of these phenolic metabolites. Support for this postulated pathway comes from in vitro binding studies with $^{14}C$-phenylethylene glycol (label unspecified), which indicate that activated rat liver microsomes catalyzed the covalent binding of this compound (blocked at the hydroxyl positions) to microsomal proteins. It is difficult to assess the biological significance of this postulated metabolic pathway, since no quantitative comparison of the amounts of phenolic metabolites to total metabolites is presented.

Seutter-Berlage and coworkers (1978) have identified mercapturic acids in the urine of rats administered 250 mg/kg styrene i.p. for fifteen days. Sulfur conjugates were found at both of the side chain carbon positions indicating prior formation of styrene oxide and glutathione attack on the ring system.

Styrene oxide was shown to be formed from styrene by rabbit liver microsomes in vitro (Leibman and Ortiz, 1969; 1970), and by microsomes from the liver, lung, and kidney of rats (Salmona et al., 1976). However, styrene oxide has not been detected in animal studies conducted in vivo. Nevertheless, it is now believed that the microsomal metabolism of alkyl-substituted aromatic compounds in general will produce unstable arene oxide intermediates (Kaubisch et al., 1976).

Studies on the metabolism of styrene oxide in the rat and rabbit indicated that both a glutathione conjugate and phenylethylene glycol are formed by the enzymatic actions of glutathione S-transferase and epoxide hydrase, respectively (Ryan and Bend, 1977; James et al., 1976). Therefore, it has been shown that styrene oxide may be an intermediate in the production of the major metabolites of styrene in vivo. The toxicologic significance of styrene oxide as an obligatory intermediate in the metabolism of styrene relates to the reputed role of epoxide metabolites in cytotoxicity and carcinogenesis by aromatic hydrocarbons (Sims and Grover, 1974). Thus, one can speculate that if the enzymatic conversion of styrene oxide to soluble metabolites is impaired or overloaded such that an accumulation of the epoxide occurs, then the potential for malignant transformation is increased.

Indeed, Sauerhoff and coworkers (1976) indicated that at high levels of styrene exposure to rats, alterations in metabolite ratios in urine were obtained. These results were indicative of dose-dependent styrene metabolism and raised the possibility that saturation of metabolism at high exposures may lead to a build-up of styrene oxide in the body. Studies on the specific toxic and mutagenic effects of styrene oxide underscore the reasons for concern regarding possible health consequences (see Sections III-B-2-f and III-B-2-g). Furthermore, recent studies have established that in the rat lung, microsomal mono-oxygenase activity for the formation of styrene oxide exceeds the activity of epoxide hydrase which degrades styrene oxide (Salmona et al., 1976). Thus, it seems likely that the lung may be a sensitive target organ for styrene toxicity. On the other hand, kinetic data for glutathione-S-transferase in the rabbit lung indicated that a very high concentration of styrene oxide would be required to saturate the enzyme (James et al., 1976). Therefore, unless a disturbance leading to glutathione depletion occurred in vivo, it is unlikely that an excess of styrene oxide would accumulate in the lung following exposure to styrene.

The relationship between reduced liver gluthathione levels produced by styrene and liver toxicity was studied in hamsters by Parkki (1978). Animals treated with 6 gm/kg intragastric styrene showed 85% depletion of liver glutathione content following sacrifice at 24 hours. Pretreatment one hour before and seven and 15 hours after styrene administration with 200 mg/kg methionine resulted in a partial protection against this depletion and reversed elevated serum alanine aminotransferase levels induced by styrene. Administration of 500 mg/kg diethyl maleate one hour before and 15 hours after styrene increased the observed alanine aminotransferase elevation, indicating a potentiating effect of sulfhydryl depletion with styrene induced liver toxicity. Based on the no effect level of styrene on liver alanine aminotransferase, a threshold value for the hepatotoxic effect of styrene was calculated to exist when glutathione content of the liver reached a level of 1 μmol/gm tissue. Thus, glutathione conjugation appears to offer significant protection against hepatotoxicity.

For many years it has been known that the metabolism of ethylbenzene involves conversion to phenylacetic acid, 1-phenylethanol, mandelic acid, and hippuric acid (Smith *et al*., 1954; El Masri *et al*., 1958). In addition, more recent studies have shown that the benzylic hydroxylation of ethylbenzene to optically active 1-phenylethanol occurs with a high degree of stereoselectivity (McMahon and Sullivan, 1966; 1968). However, the complete picture of ethylbenzene metabolism in mammals involves the participation of acetophenone and its derivatives, particularly ω-hydroxyacetophenone (Kiese and Lenk, 1973; 1974). The sequential oxidation of ethylbenzene summarized from studies conducted *in vivo* with rats indicated that the stereoselectivity of the process is probably dependent on a keto reduction step involving ω-hydroxyacetophenone or phenylglyoxal (Sullivan *et al*., 1976). The optical center of

1-phenylethanol which is formed during the initial hydroxylation of ethylbenzene is probably destroyed by a subsequent dehydrogenation step to form acetophenone.

The probable metabolic pathways involved in the biotransformation of ethylbenzene are summarized in Figure 13. It is not likely that a key epoxide intermediate is involved in ethylbenzene metabolism by mammals. It was suggested, however, that the observed formation of 2- and 4-hydroxyethylbenzene from ethylbenzene in rats (Bakke and Scheline, 1970) may be due to isomerization of the corresponding arene oxides (Kaubisch *et al*., 1972). These are minor metabolites, however, accounting for only 0.3 percent of the administered dose (Bakke and Scheline, 1970).

### c. Acute Toxicity

#### (1) Oral Administration

It has been known for many years that the acute oral toxicity of styrene, ethylbenzene, and α-methylstyrene is relatively low. This observation is consistent with the reported oral toxicities of alkylated benzenes in general. However, the acute lethal dose for the presumed styrene metabolite, styrene oxide, is somewhat lower than for the parent hydrocarbon.

Table 35 summarizes the available published data on the acute lethality of these compounds by oral administration. Pathologic examination of treated animals revealed only slight liver changes and occasional kidney involvement of questionable significance (Wolf *et al*., 1956). Intoxication by α-methylstyrene was associated with general irritation, incoordination, tremor, convulsions, and hyperemia of the internal organs (Korbakova and Fedorova, 1964). In addition, it was reported that styrene and

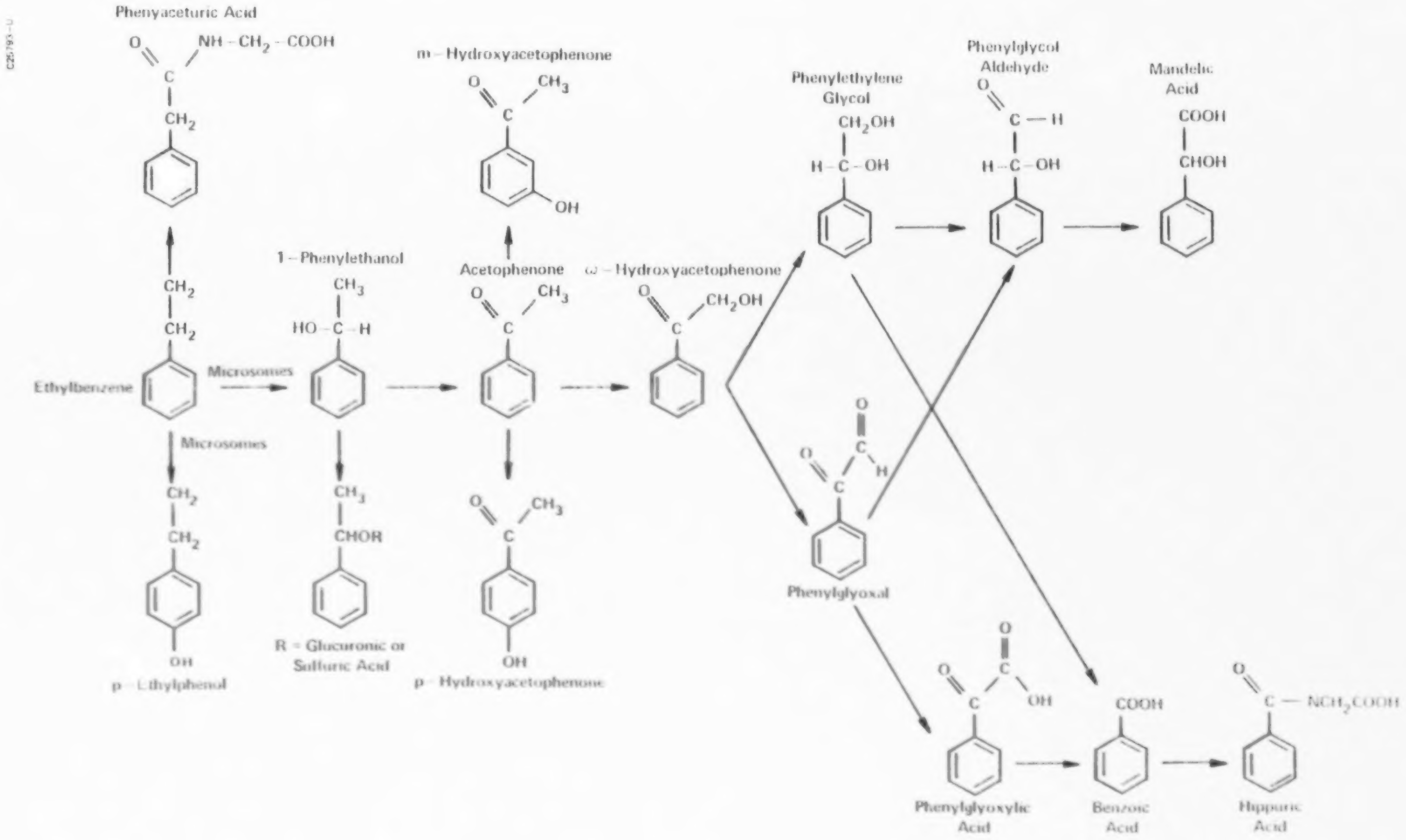

C25793-U
Phenyaceturic Acid
Ethylbenzene
Microsomes
Microsomes
p - Ethylphenol
1 - Phenylethanol
R = Glucuronic or Sulfuric Acid
m - Hydroxyacetophenone
Acetophenone
p - Hydroxyacetophenone
ω - Hydroxyacetophenone
Phenylethylene Glycol
Phenylglycol Aldehyde
Mandelic Acid
Phenylglyoxal
Phenylglyoxylic Acid
Benzoic Acid
Hippuric Acid

Figure 13. Probable Metabolic Pathways in the Biotransformation of Ethylbenzene

Table 35. Experimental Acute Oral Toxicity of Styrene and Derivatives

| Compound | Species | Sex & (No.) | Dose | Effect | Reference |
|---|---|---|---|---|---|
| Styrene | rat | male & female (57) | 5 g/kg | $LD_{50}$ (approx.) | Wolf *et al.*, 1956 |
| Styrene | rat | ? | 8 g/kg | lethal concentration | Faustov, 1960 |
| Styrene | rat | (59) | 1.6 g/kg | 100% survival | Spencer *et al.*, 1942 |
| Styrene | rat | (59) | 8.0 g/kg | 100% mortality | Spencer *et al.*, 1942 |
| Styrene Oxide | rat | male | 2.56 g/kg | $LD_{50}$ (approx.) | Weil *et al.*, 1963 |
| Ethylbenzene | rat | male & female (57) | 3.5 g/kg | $LD_{50}$ (approx.) | Wolf *et al.*, 1956 |
| Ethylbenzene | rat | ? | 6 g/kg | lethal concentration | Faustov, 1960 |
| Ethylbenzene | rat | male | $\sim$4.94 g/kg | $LD_{50}$ (range = 4.61 - 5.31 g/kg) | Smyth *et al.*, 1962 |
| α-Methylstyrene | rat | male (20) | 4.9 g/kg | $LD_{50}$ (approx.) | Wolf *et al.*, 1956 |
| α-Methylstyrene | mouse | ? | 3 g/kg | 30% mortality | Korbakova & Fedorova, 1964 |
| α-Methylstyrene | mouse | ? | 5 g/kg | $LD_{50}$ | Ogleznev, 1964 |
| α-Methylstyrene | mouse | ? | 10.25 g/kg | $LD_{50}$ | Ogleznev, 1964 |

α-methylstyrene, upon oral administration to mice and rats, caused hemodynamic and dystrophic changes in the parenchymatous organs (notably the lungs), with further morphological changes in the central nervous system characteristic of toxic encephalopathy (Zakharchenko, 1969; Veselova and Ogleznev, 1965). It is evident that species susceptibility (i.e., rats versus mice) may be a significant variable in the interpretation of acute toxicity data.

(2) Vapor Inhalation

Experiments conducted with animals acutely exposed to vapors of styrene, ethylbenzene, or α-methylstyrene indicate that the alkylated benzenes are not highly toxic. Once again, however, species susceptibility is likely to be an important factor in characterizing lethal dosage levels. Table 36 summarizes data from various studies involving single inhalation exposures.

Response to styrene vapors is usually rapid, but dependent on the severity of exposure. Rats and guinea pigs exhibit eye and nose irritation (lachrymation, salivation, nasal discharge, violent scratching) at styrene concentrations up to 1300 ppm, which is followed by general weakness and unsteadiness after 12 to 30 hours of exposure (Spencer *et al.*, 1942). Marked debilitation and occasional loss of consciousness results from 24 to 30 hours of exposure at levels of 2000 ppm. At 2500 ppm, weakness and stupor, followed by loss of equilibrium, tremors, and unconsciousness, develop within 10 to 12 hours of exposure. At 5000 ppm, reaction to styrene is immediate and involves loss of equilibrium, tremors, clonic convulsions, and unconsciousness, usually within one hour. Deaths which occur from styrene exposure are generally due to action upon the central nervous system, although delayed deaths may result from pneumonia which is secondary to acute lung irritation (Spencer *et al.*, 1942). Jaeger and coworkers (1974) attributed death in rats from

Table 36. Experimental Acute Inhalation Toxicity of Styrene and Derivatives

| Compound | Species | Sex & No. | Dose | Effect | Reference |
|---|---|---|---|---|---|
| Styrene | rat | ? | 11.8 mg/ℓ (2770 ppm) x 4 hours | $LC_{50}$ (confidence limits = 10.3-13.5 mg/ℓ) | Shugaev & Yaroslavl, 1969 |
| Styrene | rat | ? | 2700 ppm x 4 hours | $LC_{50}$ | Jaeger *et al.*, 1974 |
| Styrene | mouse | ? | 21.0 mg/ℓ (4930 ppm) x 4 hours | $LC_{50}$ (confidence limits = 17.8-24.8 mg/ℓ) | Shugaev & Yaroslavl, 1969 |
| Styrene | rat | ? | 1300 ppm | 100% survival with 30 hour exposure; 100% mortality with >40 hour exposure | Spencer *et al.*, 1942 |
| Styrene | guinea pig | ? | 1300 ppm | 100% survival with 16 hour exposure; 100% mortality with 40 hour exposure | Spencer *et al.*, 1942 |
| Styrene | rat & guinea pig | ? | 10,000 ppm | 100% survival with 1 hour exposure; 100% mortality with 3 hour exposure | Spencer *et al.*, 1942 |
| Styrene | mouse | ? | ∼3522 ppm x 2 hours | 30% mortality | Blinova & Rylova, 1957 |
| Styrene | mouse | ? | ∼2348 ppm x 2 hours | 20% mortality | Blinova & Rylova, 1957 |
| Styrene | rabbit | ? | ∼9391 ppm x 2 hours | abnormal electroencephalograms which persisted for ≤60 days | Budko & Pankovets, 1968 |
| Styrene Oxide | rat | 6 | 1000 ppm x 4 hours | death in 2 of 6 animals | Weil *et al.*, 1963 |

Table 36. Experimental Acute Inhalation Toxicity of Styrene and Derivatives (Cont'd)

| Compound | Species | Sex & No. | Dose | Effect | Reference |
|---|---|---|---|---|---|
| Ethylbenzene | rat | ? | ∿13,367 ppm x 2 hours | $LC_{50}$ | Ivanov, 1962 |
| Ethylbenzene | rat | ? | ∿16,122-17,273 ppm x 2 hours | 100% mortality | Ivanov, 1962 |
| Ethylbenzene | mouse | ? | ∿8176 ppm | $LC_{50}$ | Faustov, 1958 |
| Ethylbenzene | rat | 6 | 4000 ppm x 4 hours | 50% mortality (3/6) | Smyth et al., 1962 |
| α-Methylstyrene | mouse | ? | ∿83 ppm x 2 hours | no effect seen | Korbakova & Fedorova, 1964 |
| α-Methylstyrene | rat | ? | ∿621-1035 ppm | decrease acetylcholine level in blood, kidneys, and liver | Klimina, 1974b |
| α-Methylstyrene | mouse | ? | ∿621 ppm x 3 hours | accumulation of ammonia in the brain, reaching 2.8 times normal level within 11-20 days following exposure | Solov'ev, 1969 |
| α-Methylstyrene | rat | ? | ∿1035 ppm | increased serum vitamin $B_{12}$ level by >140%, due to liver damage | Mochkina & Bravve, 1969 |
| α-Methylstyrene | rat | ? | ∿621 ppm | reduced brain tissue respiration by >50% | Solov'ev, 1969 |

styrene inhalation to pulmonary irritation and edema. No difference in $LC_{50}$ concentrations was found when fasted or fed animals were used. Thus, the presumed reduction of hepatic glutathione levels by fasting did not enhance the toxic effects of styrene.

Target organs for acute styrene action are mainly the central nervous system, hematopoietic system, liver, lungs, and kidneys (Spencer et al., 1942; Pokrovskii, 1961). Pulmonary lesions are the predominant pathologic features of acute intoxication, varying from slight congestion to severe irritation with edema, exudation, hemorrhage, and leukocyte infiltration (Spencer et al., 1942). Guinea pigs were apparently more susceptible to pulmonary damage. Lesions of the liver and kidneys were encountered only occasionally and were usually neither severe nor persistent. Actions of styrene on the hematopoietic system include decreases in erythrocytes, thrombocytes, and hemoglobin (Pokrovskii, 1961).

Acute exposure to vapors of ethylbenzene are reportedly associated with coordination disorders, narcosis, convulsions, pulmonary irritation, and conjunctivitis (Ivanov, 1962). It is probable that the toxic mechanisms for styrene and ethylbenzene are qualitatively similar. Ethylbenzene is apparently less potent than styrene in causing death by inhalation, however.

The toxic action of α-methylstyrene when inhaled is similar to that of styrene and ethylbenzene. Degenerative changes of the cardiac muscle, liver, and kidneys have been reported (Blinova and Rylova, 1957). In addition, acute exposure to α-methylstyrene vapors can interfere with normal protein anabolism in the brain (Solov'ev, 1969) and alter blood and tissue levels of acetylcholine, acetylcholinesterase, and butyrylcholinesterase (Klimina, 1974a,b).

### (3) Skin Contact

Single skin application of styrene to the ear of a rabbit produced no appreciable reaction (Spencer *et al.*, 1942). However, Blinova and Rylova (1957) reported that styrene and α-methylstyrene, when applied undiluted to the skin of animals, caused necrosis. Moreover, two applications of styrene on the shaven abdomen of rabbits produced marked irritation and some denaturation (Spencer *et al.*, 1942). In guinea pigs and rabbits, α-methylstyrene was reportedly highly sensitizing and slightly irritating (Cirstea *et al.*, 1966).

Ethylbenzene was shown to produce moderate irritation to the uncovered belly of rabbits (Smyth *et al.*, 1962), and also to intact and abraded rabbit skin under 24-hour occlusion (Opdyke, 1975). Smyth and coworkers (1962) reported a single skin penetration $LD_{50}$ value for ethylbenzene in rabbits to be 17.8 ml/kg.

### (4) Eye Contact

Wolf and coworkers (1956) determined the eye injury potential of styrene, ethylbenzene, and α-methylstyrene in rabbits. Two drops of the undiluted material were applied to the rabbit's eye, and observations of resulting injury made periodically for seven days. Their results are summarized in Table 37.

### (5) Other Routes

Parenteral administration of styrene to male and female rats has been used to compare its toxicity with that of the presumed metabolite, styrene oxide (Ohtsuji and Ikeda, 1971). As Table 38 indicates, a sex-related difference in susceptibility to either compound does not appear to exist. However, it is clear that styrene oxide is considerably more toxic than

Table 37. Irritation and Injury to the Eyes of Rabbits Caused by Contact with Undiluted Materials[a]

| Material | Eye Response | |
|---|---|---|
| | Conjunctival Irritation[b] | Corneal Injury[c] |
| Ethylbenzene | Slight | None |
| Styrene | Moderate | Slight, transient |
| α-Methylstyrene | Slight | None |

[a] Modified from Wolf et al., 1956.

[b] The degrees of irritation were defined as follows:
slight=perceptible irritation of the conjunctival membranes
moderate=inflammation and slight swelling of the eyelids

[c] The degrees of corneal injury were defined as follows:
very slight=questionable or just perceptible superficial necrosis in very small areas of the cornea
slight=perceptible superficial necrosis involving less than 50% of the cornea
moderate=definite superficial necrosis over more than 50% of the cornea

Table 38. Intraperitoneal $LD_{50}$ Values for Styrene and Styrene Oxide in Rats[a,b]

| Sex | Expt. No. | Compounds tested<br>Styrene (g/kg) | <br>Styrene oxide (g/kg) |
|---|---|---|---|
| Male | 1 | 2.36 | 0.61 |
| | 2 | 2.15 | 0.46 |
| Female | 1 | 2.86 | 0.50 |
| | 2 | 2.41 | 0.61 |

[a] Ohtsuji and Ikeda, 1971.

[b] Based on deaths occurring within 48 hours of treatment.

styrene when administered by injection. These results would indicate, therefore, that the acute toxicity of styrene is probably mediated by styrene itself and not by formation of the epoxide metabolite.

The effects of styrene on central nervous system function in rabbits have been studied by Larsby and coworkers (1978). A 10% styrene emulsion was infused at a constant rate into the jugular vein, and arterial and cerebral spinal fluid (CSF) levels were monitored. Animals were tested for both positional and rotatory nystagmus responses (involuntary eye movements) as a measure of vestibular and oculomotor central nervous system function. At levels of 40 ppm arterial styrene, or approximately 2 ppm CSF styrene, a positional nystagmus was elicited that was not seen in controls. In addition, at comparable styrene levels a reversal of rotary nystagmus was noted. The authors commented that this reversal is an unusual effect which, to their knowledge, has not been noted with any other compound tested.

The aspiration hazard toxicity of petroleum distillates is an important consequence of accidental ingestion. Gerarde (1963) surveyed a large number of hydrocarbons for their aspiration toxicity in male rats. He found that instillation of 0.25 ml of ethylbenzene into the lungs of rats caused central nervous system stimulation, cardiac arrest, respiratory paralysis, and immediate death; this is comparable to the toxicity of benzene and toluene administered by the same route.

A technique using the chick embryo as a test system has been used to determine the relative toxicities of volatile chemicals (McLaughlin _et_ _al_., 1964). Among the chemicals tested for their ability to prevent the hatching of fertile chicken eggs (acetone, allyl alcohol, benzene, butyl acetate, _n_-butyl alcohol, carbon tetrachloride, dimethylformamide, ethyl acetate, ethyl alcohol, isoamyl alcohol, isopropyl alcohol, methanol, styrene, and toluene), styrene was second in toxicity to allyl alcohol. A dose of 18 mg styrene injected per egg completely inhibited hatching.

### d. Subchronic Toxicity

#### (1) Oral Administration

Among the earliest investigations on the toxicity of styrene by repeated oral administration is the work of Spencer and coworkers (1942) using male rats. Doses of 2000, 1000, 500, and 100 mg/kg were administered five days per week for four weeks. At the lowest dosage, all five rats survived the treatment with no apparent toxic effects and with no significant lesions at autopsy. At the 500 mg/kg dose level, reduced weight gains were evident. At the two highest dosages, a few deaths occurred which were attributed to severe irritation of the esophagus and stomach.

Subsequent studies involving repeated feedings of styrene were conducted with female rats (10 per group) given doses of 66.7 to 667 mg/kg five times per week for six months (Wolf *et al.*, 1956). Additional groups of rats were also treated with ethylbenzene at doses up to 680 mg/kg using the same treatment schedule. The results of these studies are summarized in Table 39. Only ethylbenzene induced histopathologic lesions. These consisted of cloudy swelling in hepatic parenchymal cells and renal tubular epithelium. Although hematologic parameters were evaluated (total erythrocytes and leukocytes, hemoglobin content, white blood cell count), neither compound produced any changes when compared to control animals.

A more recent report abstracted from the Russian literature indicates that when styrene is fed to rabbits at doses up to 250 mg/kg for up to 216 days, the immunological defense system is severely

Table 39. Summary of Repeated Oral Feeding of Styrene and Ethylbenzene to Female Rats[a]

| Material | Dose, mg/kg/day | Feedings, No. | Experimental Period, Days | Effects[b] |
|---|---|---|---|---|
| Ethylbenzene | 13.6 | 130 | 182 | No effect |
| | 136 | 130 | 182 | No effect |
| | 408 | 130 | 182 | Lw+ and Kw+; Lp+ and Kp+ |
| | 680 | 130 | 182 | Lw+ and Kw+; Lp+ and Kp+ |
| Styrene | 66.7 | 132 | 185 | No effect |
| | 133 | 132 | 185 | No effect |
| | 400 | 132 | 185 | G+; Lw+ and Kw+ |
| | 667 | 132 | 185 | G++; Lw++ and Kw+ |

[a] Modified from Wolf *et al.*, 1956.

[b] L=liver
K=kidney
G=growth depression
w=average weight
p=histopathology
+=slight effect
++=moderate effect

impaired (Sinitskii, 1969). The blood complement titre was reduced and leukocyte phagocytic activity was depressed.

It was reported that oral administration of 0.005 or 0.5 mg/kg of α-methylstyrene for periods of 20 to 140 days produced no permanent changes in experimental animals (species not indicated) (Ogleznev, 1969).

(2) Vapor Inhalation

Extensive studies were conducted many years ago at the Dow Chemical Company on the inhalation toxicity of styrene, ethylbenzene, and α-methylstyrene to rats, guinea pigs, rabbits, and Rhesus monkeys (Spencer et al., 1942; Wolf et al., 1956).

Animals were exposed to styrene vapors for seven to eight hours per day, five days a week, for up to six months. Maximum exposure levels employed were 2000 ppm for rats, guinea pigs, and rabbits, and 1300 ppm for monkeys. Routine hematologic and tissue examinations were conducted on animals of all species tested. Results are summarized in Table 40. No exposure-related deaths among rats resulted from any of the styrene concentrations tested; however, eye and nose irritation were commonly encountered. Among the guinea pigs exposed to styrene, 10% of those at the highest dose level died, revealing severe lung irritation with congestion, hemorrhage, edema, exudation, and a general acute inflammatory reaction. No lesions were found in other guinea pig tissues. Rabbits and monkeys were generally unaffected by repeated styrene inhalation and revealed no significant histopathologic lesions. The hematopoietic system was also apparently unaffected by styrene exposure.

Repeated inhalation exposures to ethylbenzene produced more severe reactions than exposures to similar concentrations of styrene (Wolf et al., 1956). Maximum concentrations employed were 2200 ppm for rats,

Table 40. Results of Repeated Vapor Inhalation Studies on Animals Exposed to Styrene[a]

| Animal Species | Average Vapor Concentrations, ppm | mg/ℓ | Sex & No. | 7-Hour Exposures, No. | Duration of Experiment, Days | Effects[b] |
|---|---|---|---|---|---|---|
| Rat | 2,000 | 9.3 | Both (25) | 105 | 148 | Eye and nasal irritation G++ |
| | 1,300 | 6.0-6.3 | Both (50) | 139 | 214 | Eye and nasal irritation |
| Guinea pig | 2,000 | 9.3 | Both (12) | 98 | 148 | Eye and nasal irritation G++ |
| | 1,300 | 6.0-6.3 | Both (94) | 139 | 214 | Eye and nasal irritation G+ |
| | 650 | 3.0 | Both (24) | 130 | 189 | No effect |
| Rabbit | 2,000 | 9.3 | Both (2) | 126 | 148 | No effect |
| | 1,300 | 6.0-6.3 | Both (12) | 264 | 360 | No effect |
| Rhesus monkey | 1,300 | 6.0-6.3 | Both (4) | 264 | 360 | No effect |

[a] Modified from Wolf *et al.*, 1956.

[b] G=growth depression
+=slight
++=moderate

1250 ppm for guinea pigs and rabbits, and 600 ppm for monkeys. Exposures were conducted for seven to eight hours per day, five days a week. The apparent no-effect level of exposure for physiological reactions was about 400 ppm for rabbits, guinea pigs, and monkeys (Table 41). However, this concentration proved somewhat detrimental to rats. At higher concentrations, histopathologic lesions were evident in the liver and kidneys of rats (cloudy swelling) and in the testes of rabbits and monkeys (degeneration of the germinal epithelium). No effects were demonstrated on the hematopoietic system of any species.

Exposure to α-methylstyrene, under the same conditions as for styrene and ethylbenzene reported above, indicated that a no-effect level existed in the area of 200 ppm (Table 42) (Wolf et al., 1956). In contrast to the other two chemicals, however, α-methylstyrene produced significant mortality at concentrations of 600 ppm (rabbit) and 3,000 ppm (rat and guinea pig). Nevertheless, histopathologic lesions or hematologic alterations were not reported.

The foreign literature contains numerous reports on the toxicologic effects of styrene, ethylbenzene, and α-methylstyrene in laboratory animals resulting from repeated inhalation exposures. These studies are summarized in Table 43. For the most part, it is evident that metabolic disturbances occur from exposure to styrene or α-methylstyrene, particularly in the central nervous system. In addition, styrene appears to have an adverse effect on the state of the immune system. Ethylbenzene, on the other hand, may affect hematopoiesis during long-term exposures. The clinical significance of these chemical-related disturbances is difficult to assess, however.

Table 41. Results of Repeated Vapor Inhalation Studies on Animals Exposed to Ethylbenzene[a]

| Animal Species | Average Vapor Concentrations, ppm | mg/ℓ | Sex | 7-Hour Exposures, No. | Duration of Experiment, Days | Effects[b] |
|---|---|---|---|---|---|---|
| Rat | 2,200 | 9.5 | M | 103 | 144 | G++; Lw+; Kw++; Lp+; Kp+ |
| | 1,250 | 5.4 | Both | 138 | 214 | G±; Lw+; Kw+; Lp+; Kp+ |
| | 600 | 2.6 | Both | 130 | 186 | Lw+; Kw+ |
| | 400 | 1.7 | Both | 130 | 186 | Lw+; Kw+ |
| Guinea pig | 1,250 | 5.4 | F | 138 | 214 | G+ |
| | 600 | 2.6 | Both | 130 | 186 | Lw+ |
| | 400 | 1.7 | Both | 130 | 186 | No effect |
| Rabbit | 1,250 | 5.4 | F | 138 | 214 | |
| | 600 | 2.6 | Both | 130 | 186 | Tp+ |
| | 400 | 1.7 | Both | 130 | 186 | No effect |
| Rhesus monkey | 600 | 2.6 | Both | 130 | 186 | Lw+ Tp+ |
| | 400 | 1.7 | F | 130 | 186 | No effect |

[a] Wolf et al., 1956.

[b] G=growth depression
w=weight
p=histopathology
L=liver
K=kidney
T=testes

The intensity of response is noted as follows:
±=questionable
+=slight
++=moderate

Table 42. Results of Repeated Vapor Inhalation Studies on Animals Exposed to α-Methylstyrene[a]

| Animal Species | Average Vapor Concentrations, | | Sex | 7-Hr. Exposures, No. | Duration of Experiment, Days | Effects[b] | | | |
|---|---|---|---|---|---|---|---|---|---|
| | ppm | mg/ℓ | | | | | | | |
| Rat | 3,000 | 14.49 | Both | 3-4 | 3-4 | | | | M+++ |
| | 800 | 3.86 | Both | 28 | 38 | G+; | Lw+; | Kw+ | |
| | 600 | 2.90 | Both | 149 | 212 | | Lw+; | Kw+ | |
| | 200 | 0.97 | Both | 139 | 197 | | | No effect | |
| Guinea pig | 3,000 | 14.49 | Both | 3-4 | 3-4 | | | | M+++ |
| | 800 | 3.86 | Both | 27 | 38 | G+; | Lw+; | Kw+ | |
| | 600 | 2.90 | Both | 144 | 212 | | Lw+ | | |
| | 200 | 0.97 | Both | 139 | 197 | | | No effect | |
| Rabbit | 600 | 2.90 | Both | 152 | 212 | G+; | | | M+ |
| | 200 | 0.97 | Both | 139 | 197 | | | No effect | |
| Rhesus monkey | 600 | 2.90 | F | 149 | 212 | | | No effect | |
| | 200 | 0.97 | Both | 139 | 197 | | | No effect | |

[a] Wolf *et al.*, 1956

[b] G=growth depression
w=weight
p=histopathology
L=liver
K=kidney
M=mortality

Intensity of response is noted as follows:
+=slight
++=moderate
+++=severe

Table 43. Experimental Subchronic Inhalation Exposure to Styrene, α-Methylstyrene, and Ethylbenzene

| Compound | Species | Concentration | Duration | Effects | Reference |
|---|---|---|---|---|---|
| Styrene | rat | ∿11.5 ppm | 5 hours daily x 6 months | Reduced liver glycogen, albumin-to-globulin ratio, and blood pressure; increased liver weights and altered motor function. | Zlobina, 1963 |
| Styrene | rabbit | ∿11.7 ppm | 2 hours daily x 4 months | No effect on white blood cells; toxic granulation in neutrophils; decreased hemoglobin levels; retarded maturation of myeloid cells. | Pokrovskii & Vulchkova, 1968 |
| Styrene | rabbit | ∿1.1 ppm | 4 months | Increased β-lipoprotein, cholesterol, lecithin, and nitrogen in the blood. | Pavlova & Agamova, 1974 |
| Styrene | rat | ∿1.2 ppm | 30 days | Decreased brain levels of glutamic acid, serine, and threonine; increased brain glycine levels. | Aliev & Gadzhiev, 1973 |
| Styrene | rat | ∿117 ppm | 5 hours daily x 14-30 days | Increased brain levels of free glutamate, histidine, citrulline, asparagine, serine, proline, methionine, and leucine. | Gadzhiev & Aliev, 1974 |
| Styrene | mouse,<br>rat,<br>rabbit | ∿2.3 ppm | up to 4 months | Disturbances of phagocytic mechanisms in the destruction of bacteria and assimilation of debris. | Kazakova, 1971a |

Table 43. Experimental Subchronic Inhalation Exposure to Styrene, α-Methylstyrene, and Ethylbenzene (Cont'd)

| Compound | Species | Concentration | Duration | Effects | Reference |
|---|---|---|---|---|---|
| Styrene | rabbit | $\sim$6.8 ppm | 4 hours daily x 4 months | Decreased phagocytic activity of the leukocytes and the complement titre in the serum. | Bekeshev, 1974 |
| Styrene | rabbit | $\sim$37-47 ppm | 4 hours daily x 4 months at 30-32°C | Decreased immunobiologic reactivity; decreased levels of albumins and increased levels of γ-globulins in serum. | Samedov et al., 1974 |
| Styrene | rat | $\sim$8.2 ppm | 4 hours daily, 5 times per week x 1-4 months | Lowered neutrophil phagocytic activity and greater susceptibility to staphylococcal infections. | Kazakova, 1971b |
| Styrene | rabbit | $\sim$235 ppm | 7 hours per day | Increase in abnormal pseudosinophils, monocytes, and reticulocytes. | Blinova & Rylova, 1957 |
| Styrene | rat | $\sim$1 or 12 ppm | 1-4 months | Changes in duration of the estrous cycle. | Izyumova et al., 1972 |
| α-Methylstyrene | rat | $\sim$10.3 ppm | 4-5 hours daily x 6 months | Increased degradation and deamination of brain proteins; uncoupling of oxidative phosphorylation in the brain | Solov'ev, 1974 |
| α-Methylstyrene | rat | $\sim$8.3-14.5 ppm | 1-4 months | Increased acetylcholine in the brain and kidneys and decreased acetylcholine in the blood and liver during the first month; decreased acetylcholinesterase in the blood and spleen. | Klimina, 1974a |

Table 43. Experimental Subchronic Inhalation Exposure to Styrene, α-Methylstyrene, and Ethylbenzene (Cont'd)

| Compound | Species | Concentration | Duration | Effects | Reference |
|---|---|---|---|---|---|
| α-Methylstyrene | rat | $\sim$0.54 ppm | 6 hours per day x 120 days | Vascular disorder in the brain stem and damage to neurons and neuroglia. | Zakharchenko, 1969 |
| α-Methylstyrene | rat | $\sim$1-20 ppm | 120 days | Altered lipid metabolism; increased liver cholesterol from 119 to 246.2 mg %. | Chukreev, 1969 |
| α-Methylstyrene | rat | $\sim$1.2 ppm | 6 hours per day, 6 days per week x 4 months | Damage to respiratory epithelium; hypersecretion of epithelial mucins; damaged blood vessel permeability. | Kuz'min, 1969a, 1969b |
| α-Methylstyrene | rat | $\sim$10.3 ppm | "chronic" | Increased erythrocyte volume by 11-37% and increased hemolysis. | Mochkina & Bravve, 1969 |
| α-Methylstyrene | rat | $\sim$621 ppm | 3 hours per day x 100 days | Abscesses of lung and hypodermic tissue; pneumonia, and splenic hyperplasia in rats on a protein and vitamin-deficient diet. | Blinova & Rylova, 1957 |
| α-Methylstyrene | rat | $\sim$2.1-8.3 ppm | 5 hours per day x 7 months | Lowered urine volume and increased urinary protein; hyperplasia of lymphatic follicles; increased number of lung histiocytes; perivascular histiocyte infiltration; lipid dystrophy in the liver. | Korbakova & Fedorova, 1964 |
| α-Methylstyrene | rat | $\sim$1 ppm | 6 hours per day x 120 days | Inhibition of lymphopoiesis. | Molodyuk, 1969 |

Table 43. Experimental Subchronic Inhalation Exposure to Styrene, α-Methylstyrene, and Ethylbenzene (Cont'd)

| Compound | Species | Concentration | Duration | Effects | Reference |
|---|---|---|---|---|---|
| Ethylbenzene | rabbit | ∿230 ppm | 4 hours per day x 7 months | Muscle chronaxia changes; disturbed blood cholinesterase activity; decreased plasma albumin; increased plasma globulins; leukocytosis; reticulocytosis; cellular infiltration; lipid dystrophy in the liver; dystrophic changes in the kidneys. | Ivanov, 1964 |

### (3) Skin Contact

Repeated skin contact with styrene, α-methylstyrene, or ethylbenzene is not well-tolerated in experimental animals. Ten to twenty applications of either styrene or ethylbenzene to rabbits' skin caused a definite erythema with development of a thin layer of devitalized tissue (Wolf *et al*., 1956). A similar treatment using α-methylstyrene produced a more morbid erythema, also accompanied by slight tissue necrosis. Absorption of these compounds through the skin in amounts sufficient to be acutely toxic did not occur.

A report on studies conducted in Russia (Mirzoyan and Zhakenova, 1972) indicates that α-methylstyrene (30%) applied for twenty days to rabbit skin resulted in inflammation, hyperemia, edema, and desquamation. In addition, sensitization was reported.

### (4) Parenteral Administration

Several reports abstracted from the foreign literature suggest that subchronic administration of styrene by injection is associated with disturbances in biochemical parameters of nervous system function and possible effects on the liver. These studies are summarized in Table 44.

## e. Teratogenicity

Studies concerning the embryotoxic and teratogenic potential of styrene have only recently been conducted. No information is available concerning the possible effects of α-methylstyrene or ethylbenzene on reproduction.

Investigators at the Dow Chemical Company treated groups of pregnant female rats on days six to fifteen of gestation with styrene monomer

Table 44. Subchronic Effects of Styrene Administered by Injection to Experimental Animals

| Species | Dose | Route | Duration | Effect | Reference |
|---|---|---|---|---|---|
| Rat | 2.5 g/kg/day | injection | up to 20 days | Suppression of serotonin metabolism; decreased tissue monoamine oxidase activity and increased levels of ceruloplasmin; decreased excretion of 5-hydroxyindale-3-acetic acid. | Askalalonov, 1977 |
| Rat | 2.5 g/kg/day | subcutaneous injection | 15-20 days | Decreased level of serotonin in the blood, lungs, brain, and intestine. | Askalonov, 1973a |
| Rabbit | 600 mg/kg/day | subcutaneous injection | 3-10 days | Increased activity of serum cholinesterase and arylesterase. | Askalonov, 1973b,c |
| Rabbit | 250 mg/kg/day | intraperineal injection | until death resulted | Increased serum levels of globulin, glycoprotein, and lipoprotein. | Pannain & Scala, 1960 |

by gavage (Murray et al., 1976). Styrene was administered twice daily in doses of either 90 or 150 mg/kg, constituting a total daily dose of 180 or 300 mg/kg. No evidence was obtained to indicate a styrene-related teratogenic effect. No increases were seen in the incidence of skeletal or soft tissue abnormalities, or in pregnancy rate, litter size, fetal body weight, or fetal viability. At both dose levels, however, maternal toxicity was observed, which consisted of weight loss and decreased food consumption. At the higher dosage, styrene treatment produced focal ulceration in the gastric wall of pregnant rats.

The teratogenic effects of styrene and styrene oxide on developing chick embryos has been studied by Vainio and coworkers (1977). Styrene at 52-520 mg/egg and styrene oxide at 64-320 mg/egg were injected into the air space of fertilized eggs on day zero and day one of incubation. Embryos were examined on day 14 and scored for malformations. The average incidence of malformations in styrene injected eggs was 15%, while for styrene oxide injected eggs the average incidence was 7%. No malformations were observed in vehicle injected controls. Malformations included a wide variety of types with no single anomaly predominating. The significance of these data is difficult to assess. At the higher concentrations of compound tested, levels in excess of the $LD_{50}$ value were being employed. Growth retardation observed in treated embryos confirms the toxicity of this schedule. Since only average incidence of malformations was presented, no correlation between dose and effect can be made.

Pagano and coworkers (1978) have investigated the teratogenic effects of styrene and styrene oxide on the developing sea urchin egg. Either eggs or sperm were pretreated before fertilization for 1-2 minutes and then extensively washed, or the fertilized eggs were treated at different stages of in the continued presence of chemical. Concentrations of $10^{-4}$ M styrene resulted in a 30% incidence of abnormal embryos. Styrene oxide at $10^{-4}$ to $10^{-5}$ M concentrations also produced abnormalities of differentiation when given before or after fertilization; no quantitative data were presented for the incidence of these effects. The authors state that the effects seen resemble those produced by weak mutagens in this assay system.

Recently the results of studies conducted on rats and rabbits to determine the teratogenic effects of styrene have been reported (Murray, et al., 1978). Rats and rabbits were exposed to 300 and 600 ppm styrene vapor for 7 hours/day during gestation (day 6-15 in rats, days 6-18 in rabbits). Additional groups of rats were fed 90 or 150 mg/kg by gavage twice daily during the same gestation interval. A few minor skeletal deformities (lumbar spurs, delayed ossification) were seen in the rats exposed to 300 ppm, but not at the 600 ppm exposure level. At this level (300 ppm) rats also showed decreased embryo length. Rabbits showed some delayed ossification at the 600 ppm exposure level. No other deformities or reproductive effects were seen. Since rabbits appear to be less sensitive to styrene inhalation than rats, studies at higher levels may be indicated.

In contrast to these results, the Russian literature contains a report of embryotoxic effects resulting from styrene inhalation during the entire gestation period (Ragule, 1974). Exposure of pregnant rats to approximately 0.4 to 12 ppm styrene four hours daily throughout gestation caused a decreased number of offspring and a lowered viability of newborns. The significance of exposure route in this study may be an important factor in comparing these results to those reported by Murray and coworkers (1976).

### f. Mutagenicity

Significant concern regarding the safety of styrene has arisen as the result of studies which indicated that styrene and its metabolites possess mutagenic activity in certain test systems. By virtue of its biotransformation to styrene oxide, a possible carcinogen (see Section III-B-2-g), styrene has been considered as a likely candidate for mutagenicity testing. Reports are now available on the mutagenicity of both styrene and styrene oxide in eukaryotic and prokaryotic cell systems.

The simple *Salmonella* (± microsome) microbial test for mutagenesis has produced results which are somewhat difficult to interpret. Styrene oxide has conclusively been shown to directly induce mutations in tester strains which detect base-pair substitutions (Vainio *et al.*, 1976; Stoltz and Withey, 1977; Milvy and Garro, 1976) (Tables 45 and 46). In addition, styrene was reportedly not mutagenic to *Salmonella* in the absence of a microsomal activating system (Milvy and Garro, 1976) (Table 45). Incubation of styrene in the presence of liver microsomes, however, has produced both positive (Vainio *et al.*, 1976; DeMeester *et al.*, 1977) and negative (Stoltz and Withey, 1977) results (Tables 47 and 48). The lack of mutagenic effect by styrene in the presence of liver microsomes may have been due to poor conversion of styrene to the epoxide and/or the rapid removal of styrene oxide once it was formed. Nevertheless, it can be concluded from the work of Milvy and Garro (1976) that the mutagenicity of styrene to *Salmonella* strains TA 1535 and TA 100 is probably due to styrene oxide and not caused by other styrene metabolites (Table 45).

Watabe and coworkers (1978) have studied increased mutagenicity produced by styrene and styrene oxide under various conditions in the

Table 45. Mutagenicity of Styrene and Its Metabolites For *Salmonella typhimurium*[b]

| COMPOUND[a] | Revertants per plate | | | | |
|---|---|---|---|---|---|
| | TA1535 | TA100 | TA1537 | TA1538 | TA98 |
| Styrene | 61 | 268 | 8 | 5 | 1 |
| Styrene oxide | 535 | 2694 | 10 | 19 | 6 |
| Styrene glycol | 93 | 300 | 5 | 12 | 14 |
| D mandelic acid | 106 | 267 | 7 | 1 | 10 |
| L mandelic acid | 153 | 492 | 2 | 17 | 8 |
| Phenylglyoxylic acid | 162 | 309 | 5 | 16 | 6 |
| Benzyl alcohol | 177 | 411 | 11 | 25 | 10 |
| Benzoic acid | 101 | 297 | 12 | 3 | 12 |
| Hippuric acid | 186 | 342 | 0 | 8 | 18 |
| Spontaneous | 135 | 331 | 5 | 14 | 26 |

---

[a] The test compounds were applied either as 5 μl of liquid (styrene, styrene oxide and benzyl alcohol) or in approx. 100 μg amounts of solid to the center of agar overlay plates seeded with the tester strains indicated. The sources of the chemicals were: styrene and styrene oxide, Eastman Organic Chemicals; styrene glycol, benzyl alcohol and hippuric acid, Biochemical Laboratories; D and L mandelic acids and phenylglyoxylic acid, Aldrich Chemical Co.; benzoic acid, Mallinckrodt Chemical Works. The styrene oxide is estimated by the manufacturer, Union Carbide Chemical Corp., to be 97-98% pure.

[b] Milvy and Garro, 1976.

Table 46. Mutagenicity of Styrene Oxide to Salmonella typhimurium (-- indicates the absence and + the presence of 0.1 ml of S-9 per plate)[a]

| Concentration of styrene oxide moles/plate | TA 1535 -- | TA 1535 + | TA 1537 -- | TA 1537 + | TA 1538 -- | TA 1538 + | TA 100 -- | TA 100 + | TA 98 -- | TA 98 + |
|---|---|---|---|---|---|---|---|---|---|---|
| $10^{-4}$ | toxic | | toxic | | toxic | | toxic | | toxic | |
| $10^{-5}$ | 357 | 484 | 8 | 8 | 11 | 32 | 1111 | 1165 | 25 | 26 |
| $10^{-6}$ | 425 | 468 | 6 | 8 | 7 | 35 | 443 | 639 | 26 | 16 |
| $10^{-7}$ | 249 | N.D.[b] | N.D. | N.D. | 9 | 16 | 217 | 146 | 16 | 16 |
| $10^{-8}$ | 124 | N.D. | N.D. | N.D. | 5 | 12 | 240 | 142 | 8 | 19 |
| $10^{-9}$ | 19 | 18 | N.D. | N.D. | 7 | 9 | 115 | 108 | 11 | 13 |
| 0 | 20 | 45 | 7 | 4 | 9 | 7 | 84 | 135 | 26 | 21 |

---

[a] Vainio *et al.*, 1976.

[b] No data

Table 47. Mutagenicity of Styrene to *Salmonella typhimurium* (- indicates the absence and + the presence of 0.1 ml of S-9 per plate).[a]

| Concentration of styrene moles/plate | TA 1535 | | TA 1537 | | TA 1538 | | TA 100 | | Ta 98 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | - | + | - | + | - | + | - | + | - | + |
| $10^{-4}$ | toxic | | toxic | | toxic | | toxic | | toxic | |
| $10^{-5}$ | | | | | | | | | | |
| $10^{-6}$ | 13 | 16 | 7 | 11 | 8 | 10 | 197 | 206 | 21 | 24 |
| $10^{-7}$ | 20 | 84 | 12 | 12 | N.D.[b] | N.D. | 56 | 78 | N.D. | N.D. |
| $10^{-8}$ | 22 | 112 | N.D. | N.D. | N.D. | N.D. | 115 | 163 | N.D. | N.D. |
| 0 | 17 | 16 | 7 | 12 | 9 | 7 | 83 | 97 | 24 | 13 |

---

[a] Vainio *et al.*, 1976.

[b] No data

Table 48. Lack of Reversion of S. typhimurium TA1535 by Styrene in the Presence of Different Amounts of Fortified Liver Homogenates from Arochlor 1254-pretreated Rats and Hamsters [a]

| Treatment | mg microsomal protein/plate | Revertants/plate Rat | Revertants/plate Hamster |
|---|---|---|---|
| 20% EtOH | 0 | 12.3 | 16.3 |
| | 1 | 14.0 | 15.6 |
| | 2 | 16.0 | 11.0 |
| | 3 | 12.3 | 12.0 |
| Styrene<br>500 μg/plate | 0 | 8.3 | 9.7 |
| | 1 | 9.3 | 10.7 |
| | 2 | 15.0 | 12.7 |
| | 3 | 15.7 | 10.0 |
| DMSO | 0 | 10.7 | 12.0 |
| | 1 | 5.7 | 6.0 |
| | 2 | 6.7 | 5.0 |
| | 3 | 7.7 | 7.3 |
| β-Naphthylamine<br>2 μg/plate | 0 | 13.3 | 11.3 |
| | 1 | 226.3 | 137.3 |
| | 2 | 284.7 | 75.7 |
| | 3 | 168.0 | 56.3 |

[a] Stoltz and Withey, 1977.

Ames assay. Styrene added to the test system at 10-500 mg/plate failed to induce mutations in any tester strain when an S-9 microsomal extract prepared from the livers of Aroclor treated rats was added. Styrene oxide increased mutations in the Ames assay without S-9 activation at levels of 100 mg/plate and higher. If S-9 extract prepared from phenobarbital or methylcholanthrene treated rats was used, and an inhibitor of epoxide hydrase activity, trichloprene oxide (TCPO) was included, styrene added to the assay at 600 and 1200 mg/plate induced a higher mutation rate in tester strain TA 100. Under these conditions methylcholanthrene treated rats were the best source of S-9 liver preparation for activation. Addition of this S-9 preparation to the Ames system (TA 100) containing styrene oxide abolished the mutagenic activity of this compound. Further addition of TCPO partially restored the mutagenic activity, indicating that epoxide breakdown caused by the S-9 mix was a contributing factor to the lack of activity noted. The authors speculate that since Aroclor treated liver preparation is effective in converting styrene to styrene oxide but ineffective in promoting styrene mutagenesis even in the presence of TCPO, another active styrene metabolite is probably the mutagenic agent in this system. 4-Vinyl phenol was tested for mutagenicity but was found to have a potent killing effect, making evaluation of its effects not possible. Positive results observed should be considered relative to the assay procedure. The activation of styrene using S-9 mixture incubated for 20 minutes with TCPO was carried out by further incubation with bacterial cells at 37° for 20 minutes in a shaker bath before addition to agar and plating. This modification of the Ames procedure is more effective in activating compounds that show borderline mutagenic activity than the standard technique. Busk (1979) was unable to show mutagenic effects of styrene on tester strains TA 100 and TA 1535 at concentrations up to 15 μmoles/plate.

Styrene oxide, at levels of 1-10 μ moles/plate was mutagenic in both tester strains. Aroclor or PCB induced microsome preparations did not activate styrene and increase Salmonella mutations, nor did the further addition of TCPO or diethyl maleate to the test system increase mutation rate. The standard Ames technique was used for all testing. This group did not use TCPO addition in the TA 100 strain assays because of reported high mutagenicity of this compound itself for the TA 100 strain. Thus, comparison of the Watabe results with those obtained by Busk is not possible.

Further studies conducted in test systems which employ eukaryotic cells (yeast and hamster) have confirmed the mutagenic properties of styrene oxide. Investigators in Italy (Loprieno _et al_., 1976a,b; Abbondandolo _et al_., 1976) tested styrene and styrene oxide for their mutagenic effect on a gene conversion system of yeast (_S. cerevisiae_), and on a forward mutation system of Chinese hamster cells and yeast (_S. pombe_). Styrene was tested either directly or after its biotransformation by liver microsomes _in vitro_ or by host-mediated metabolism _in vivo_. Styrene oxide was found to be active in the production of forward mutations in both yeast and hamster cells (Tables 49 and 50). Styrene, on the other hand, was inactive in yeast, even in the presence of liver microsomes (Table 49). It was assumed that the conversion of styrene to the epoxide was very low in this case. However, in the host-mediated assay, both styrene (1000 mg/kg) and styrene oxide (100 mg/kg) were active in the production of gene conversion (Table 51), but were unable to increase forward mutation frequency in yeast cells (Table 52). By comparison with the well-known mutagen ethylmethane sulfonate, the authors concluded that styrene oxide was a more potent mutagen in the production of forward mutations in cultured hamster cells. However, the high doses (1000 mg/kg) required for

Table 49. Forward Mutations (ade Mutants) Induced in Yeast S. Pombe ($P_1$ Strain)[a]

| COMPOUND | mM | Treatment Time | Survival % ± S.E.M. | Number of mutants / Number of colonies | Mutants ade$^-$ / $10^4$ colonies |
|---|---|---|---|---|---|
| Styrene | 100 | 0 | 100.0 | 1/23,430 | 0.43 |
| | (buffer) | 60' | 93.7 | 2/45,056 | 0.44 |
| | 100 | 0 | 100.0 | 2/17,424 | 1.14 |
| | (+ purified microsome) | 60' | 67.8 | 2/22,745 | 0.88 |
| Styrene oxide | 5.0 | 0 | 100.0 | 5/58,878 | 0.85 ± 0.06 |
| | | 60' | 71.3 ± 13.9 | 12/38,627 | 3.17 ± 1.04 |
| | 10.0 | 0 | 100.0 | 4/48,325 | 0.82 ± 0.16 |
| | | 60' | 41.9 ± 5.0 | 22/33,590 | 6.86 ± 3.34 |
| | 15.0 | 0 | 100.0 | 4/42,052 | 1.02 ± 0.28 |
| | | 60' | 4.6 ± 0.7 | 15/17,974 | 8.31 ± 0.02 |
| | 20.0 | 0 | 100.0 | 1/15,096 | 0.66 |
| | | 60' | 3.8 | 34/11,739 | 28.96 |

---

[a] Loprieno et al., 1976a.

Table 50. Forward Mutations (azg$^r$ Mutants) Induced in Chinese Hamster Cells ($V_{79}$ Strain)[b,c]

| COMPOUND | mM[a] concentration | Expression time of plated cells | P.E. (%) | azg$^r$ mutants | Viable cells x $10^3$ | azg$^r$/$10^6$ cells ± S.E.M. |
|---|---|---|---|---|---|---|
| Styrene | 0 | | 100 | 43(5) | 3746 | 11.37 ± 2.35 |
| | 8.5 | 66 | 83.7 | 11(2) | 1664 | 13.14 ± 0.32 |
| | 17.0 | 90 | 77.4 | 30(2) | 1394 | 20.56 ± 11.14 |
| Styrene oxide | 0 | | 89.8 | 61(13) | 12,177 | 4.94 ± 1.22 |
| | 4.25 | 72 | 72.4 | 7(2) | 1385 | 5.09 ± 0.95 |
| | 8.50 | 72 | 57.4 | 53(3) | 1721 | 29.97 ± 11.32 |
| | 17.0 | 90 | 14.9 | 32(3) | 263 | 139.96 ± 28.32 |
| | 25.0 | 90 | 20.0 | 91(1) | 200 | 455.00 |

---

[a] Treatment, 60 min.

[b] In parentheses the number of independent experiments.

[c] Loprieno *et al.*, 1976.

Table 51. Mutagenicity Test With Host-Mediated Assay (Mice)[a]: Gene Conversion (*S. Cerevisiae*, $D_4$ Strain)[c]

| COMPOUND | Dose | Locus | Incubation time (h)<br>0 | 1 | 3 | 6 |
|---|---|---|---|---|---|---|
| Styrene | Control | ade | $1.03 \pm 0.26 \times 10^{-5}$<br>(6)[b] | | | $0.92 \pm 0.69 \times 10^{-5}$<br>(3) |
| | | trp | $0.51 \pm 0.17 \times 10^{-5}$<br>(6) | | | $1.37 \pm 0.73 \times 10^{-5}$<br>(3) |
| | 1000 mg/kg | ade | | $4.23 \pm 0.72 \times 10^{-5}$<br>(3) | $4.75 \pm 0.64 \times 10^{-5}$<br>(6) | $5.38 \pm 1.37 \times 10^{-5}$<br>(5) |
| | | trp | | $1.94 \pm 0.25 \times 10^{-5}$<br>(3) | $2.50 \pm 0.35 \times 10^{-5}$<br>(4) | $2.64 \pm 0.61 \times 10^{-5}$<br>(4) |
| Styrene oxide | Control | ade | $1.00 \pm 0.07 \times 10^{-5}$<br>(3) | | | $1.18 \pm 0.11 \times 10^{-5}$<br>(3) |
| | | trp | $1.30 \pm 0.28 \times 10^{-5}$<br>(3) | | | $0.91 \pm 0.24 \times 10^{-5}$<br>(3) |
| | 100 mg/kg | ade | | $1.44 \pm 0.08 \times 10^{-5}$<br>(3) | $1.42 \pm 0.18 \times 10^{-5}$<br>(3) | $2.29 \pm 0.53 \times 10^{-5}$<br>(3) |
| | | trp | | $2.14 \pm 0.15 \times 10^{-5}$<br>(3) | $1.43 \pm 0.14 \times 10^{-5}$<br>(3) | $1.84 \pm 0.27 \times 10^{-5}$<br>(3) |

---

[a] Treatment by gavage: 1 ml of DMSO solution.

[b] Number of mice treated and analyzed.

[c] Loprieno *et al.*, 1976.

Table 52. Mutagenicity Test With Host-Mediated Assay (Mice)[a]: Forward Mutation (*S. Pombe*; ade Mutants; $P_1$ Strain)[c]

| COMPOUND | Dose | Incubation time (h)<br>0 | 3 | 6 | 12 |
|---|---|---|---|---|---|
| Styrene | Control | $1.20 \pm 0.20 \times 10^{-4}$<br>(6)[b] | | | $1.29 \pm 0.22 \times 10^{-4}$<br>(4) |
| | 1000 mg/kg | | $2.07 \pm 1.18 \times 10^{-4}$<br>(4) | $1.67 \pm 0.54 \times 10^{-4}$<br>(6) | $3.52 \pm 1.21 \times 10^{-4}$<br>(8) |
| Styrene oxide | Control | $1.16 \pm 0.15 \times 10^{-4}$<br>(7) | | | $1.21 \pm 0.22 \times 10^{-4}$<br>(3) |
| | 100 mg/kg | | $0.96 \pm 0.05 \times 10^{-4}$<br>(8) | $1.23 \pm 0.23 \times 10^{-4}$<br>(9) | $2.09 \pm 0.49 \times 10^{-4}$<br>(6) |

---

[a] Treatment by gavage: 1 ml of aqueous solution.

[b] Number of mice and analyzed.

[c] Loprieno *et al*., 1976.

styrene to exert a mutagenic effect implies that the degree of metabolic conversion to styrene oxide is a limiting factor for mutagenesis.

Sorsa (1978) has made a preliminary report on the induction of recessive lethal mutations in Drosophila following exposure to 100 ppm styrene oxide vapor (duration not specified). Styrene oxide increased (9 fold) the frequency of recessive lethals observed. Pretreatment with 1% phenobarbital for 24 hours followed by exposure to 100 ppm styrene oxide produced a four fold increase in mutations over those produced by styrene oxide treatment alone.

The mutagenic effects of styrene and styrene oxide have been tested in onion root tip cells (Allium Cepa) (Linainman *et al.*, 1978). Application of equal amounts of styrene and styrene oxide solutions (0.05%) to bulbs produced cytogenetic abnormalities. Styrene was more effective at this level in producing chromosome breaks, while styrene oxide produced a significant increase in cells with micronuclei. Both agents caused decondensation of chromatin, suggesting an effect on chromosomal proteins. Autoradiography after exposure of bulbs to 7-$^3$H styrene oxide showed covalent binding of the compound to both cytoplasmic and nuclear sites. Similar effects on chromosomes of human lymphocytes cultured *in vivo* have been noted by these investigators.

An increased incidence of chromosome aberrations has been reported (Meretoga *et al.*, 1978) in male rats exposed to 300 ppm styrene for 2-11 weeks (6 hrs/day, 5 days/wk). Aberrations seen were mainly chromosome breaks, but some chromatid breaks were also observed. These effects were seen following nine weeks of exposure. Polyploid cells were observed in preparations of bone marrow cells from animals exposed for eleven weeks. From nine to eleven weeks the incidence of aberrations in styrene treated marrow cells was 8-12% while controls showed a 1-6% incidence. Treated animals were not followed after discontinuation of exposure to determine whether these changes were readily reversible. Bonatti et al. (1977) has also noted polyploidy in cultured V79 Chinese hamster cells exposed to styrene oxide.

No information is available in the published literature concerning the mutagenicity of α-methylstyrene or ethylbenzene.

### g. Carcinogenicity

The preliminary results of a single study have been reported (Jersey et al., 1978) on the possible carcinogenicity of styrene. Rats of both sexes inhaled styrene vapors (600 or 1000 ppm) six hours daily, five days per week, for most of a two year period. Among the males a high mortality which was unrelated to the styrene exposure prevented an accurate interpretation of the data. Female rats, on the other hand, displayed an increase in tumors of lymphatic or hematopoietic origin at both exposure levels.

The incidence of combined leukemia-lymphosarcoma in female rats subjected to styrene at either 1000 ppm or 600 ppm exposure was ∿ 7% (6/85). Controls for this study showed a 1/85 occurrence of lymphosarcoma. Historial analysis of leukemia-lymphosarcoma in female controls over a five year period and comparison with styrene-treated female rats indicated a significant tumor increase.

Results of the National Cancer Institute study on the possible carcinogenicity of styrene administered by gavage to rats and mice have been reported (NCI, 1979). Rats of both sexes were administered styrene at levels of 2000 mg/kg and 1000 mg/kg, five days per week, for 78 weeks. An additional group of rats was given 500 mg/kg styrene for 103 weeks, on the same schedule. Male and female mice were administered styrene at levels of 300 mg/kg and 150 mg/kg for 78 weeks, five days per week. No statistically significant increase in any tumor type was found for male or female rats, or female mice. However, survival of both sexes of rats at the 2000 mg/kg level was low, and early mortality makes analysis of tumor incidence in this group impossible. Male mice showed an increased incidence of alveolar/bronchiolar carcinoma and adema for animals treated with 300 mg/kg styrene. This incidence (9/43 or 20.9%) is significantly higher than for vehicle controls employed in the study; however, historical controls with this strain of mice at the NCI facility show spontaneous incidences of this type of tumor in the same frequency range. Therefore, caution should be exercised in interpreting this finding in one treatment group and one sex of test animals.

Limited studies have been conducted with mice to determine the tumorigenicity of styrene oxide when applied to the skin. Weil et al. (1963) observed no tumors among 40 12-week old $C_3H$ mice painted with a 5% solution of styrene oxide three times a week for life (17 to 24 months). When a 10% styrene oxide solution was similarly applied, only two of 40 mice survived at 17 months, and no tumors were observed. Since styrene oxide is a highly reactive electrophile, it will have a reduced probability of surviving passage through the cytoplasm to reach critical cellular receptors which most likely are in the nucleus. This factor may explain the negative results for styrene oxide-induced skin tumors.

Among 30 8-week old male Swiss ICR/Ha mice painted with 0.1 ml of a 10% styrene oxide solution in benzene twice weekly for life, three (10%) developed skin tumors (Van Duuren et al., 1963). The median survival time for treated mice was 431 days. Among benzene-treated control mice 7% (11 of 150 animals) developed skin tumors.

Kotin and Falk (1963) have reported a 16% incidence (3 of 20 animals) of malignant lymphoma among $C_3H$ mice painted with a total of 20 μm styrene oxide. Nineteen of the mice survived the treatment, with the first tumor appearing after 11 months. No tumors of other sites (skin, pulmonary) were found in this study. Data were not given on the vehicle used for administration of the test compound, the incidence of tumors among controls, or the treatment schedule employed.

More recent evidence concerning the involvement of styrene oxide with neoplastic transformation was reported by Nesnow and Heidelberger (1976). In a cell culture transformation system using a $C_3H$ mouse embryo fibroblastic cell line, styrene oxide caused a two-fold increase in 3-methylcholanthrene-mediated transformation. Styrene had no effect on 3-methylcholanthrene-induced cell transformation (Table 53). The results indicated that styrene oxide may increase chemical carcinogenesis by aromatic hydrocarbons due to its ability to inhibit epoxide hydrase, a critical enzyme for the detoxification of carcinogenic arene oxide intermediates. Alternately, it was suggested that styrene oxide may increase cellular steady-state levels of oncogenic arene oxides by reacting with and thus depleting glutathione. The fact that styrene did not alter the rate of transformation in this system argues against the *in situ* formation of styrene oxide in sufficient quantities to affect transformation.

Information is not presently available regarding the potential for neoplastic transformation by direct exposure to α-methylstyrene or ethylbenzene.

Table 53. Effect of Modifiers of Microsomal Enzymes on 3-MC-Mediated Transformation and Cytotoxicity in 10T1/2CL8 Cells[g]

| 3-MC (μM) | Modifier |  |  | PE[a] | % Survival[b] | Transformation[c] | % Control |
|---|---|---|---|---|---|---|---|
|  | Concentration (μM) | Start treatment[d] | Length of treatment[e] |  |  |  |  |
| 0 |  |  |  | 30 | 100 | 0 |  |
| 3.7[f] |  |  |  | 30 | 100 | 3.4 | 100 |
|  |  | Styrene |  |  |  |  |  |
| 0 | 10 | -24 | 72 | 13 | 65 | 0 |  |
| 37 | 10 | -24 | 72 | 12 | 60 | 8.1 | 108 |
| 0 | 50 | -24 | 72 | 12 | 60 | 0 |  |
| 37 | 50 | -24 | 72 | 9 | 45 | 7.2 | 96 |
|  |  | Styrene oxide |  |  |  |  |  |
| 0 | 50 | 0 | 48 | 22 | 92 | 0 |  |
| 37 | 50 | 0 | 48 | 10 | 42 | 9.4 | 224 |
| 37 | 50 | -24 | 72 | 21 | 88 | 3.1 | 74 |

---

[a] PE, percentage of the number of colony-forming cells, relative to the number of cells seeded.

[b] Percentage of the ratio of the treated to control PE.

[c] Expressed as the number of transformed foci per dish, adjusted for PE.

[d] Start treatment refers to the time (in hr.) that the chemical was added to the cells relative to the time of 3-MC addition (zero time); thus, cells treated at -24 were treated 24 hr. prior to 3-MC addition.

[e] Length of treatment is the total time (in hr.) that the cells were in contact with the chemical.

[f] Cells were treated with 3-MC for 72 hr.

[g] Modified from Nesnow and Heidelberger, 1976.

### 3. Effects on Other Vertebrates

#### a. Fish

Both styrene and ethylbenzene have been tested for their acute toxicity to various species of fish (Pickering and Henderson, 1966). Static bioassays were conducted and median tolerance limit (TLM) values computed from the mortalities in different concentrations of toxicant occurring after 24, 48, and 96 hours of exposure. Bioassay results in four species of fish are presented in Table 54. No explanation was given for the lack of confidence limits for bluegills exposed to ethylbenzene.

A further analysis of the data obtained was made with regard to potential for cumulative toxicity, comparative susceptibility of fish species (Tables 55 and 56), and comparative toxicity in different dilution waters. It is evident from these data that species susceptibility exists to both styrene and ethylbenzene. Moreover, the toxicity of styrene was enhanced when soft water was used for dilution. No significant differences for either compound were found between the 24 and 96 hour TLM values.

No information has been found concerning the toxicity to fish or other non-mammalian vertebrates by α-methylstyrene or divinylbenzene.

### 4. Effects on Invertebrates

No information is available for any of the compounds under review.

### 5. Effects on Plants

No information is available for any of the compounds under review.

Table 54. Median Tolerance Limits for Styrene and Ethylbenzene Obtained with the Moving Average-Angle and Graphical Interpolation Methods[a]

| | | | 24-Hr. | | 48-Hr. | | 96-Hr. | | Graphical Interpolation 96-Hr. $TL_m$ (mg/1) |
|---|---|---|---|---|---|---|---|---|---|
| COMPOUND | Dilution Water | Test Fish | $TL_m$ (mg/1) | Confidence Limits (mg/1) | $TL_m$ (mg/1) | Confidence Limits (mg/1) | $TL_m$ (mg/1) | Confidence Limits (mg/1) | |
| Styrene (stabilized B.P.43-45) | Soft | Fatheads | 56.73 | 47.67-67.83 | 53.58 | 43.04-71.21 | 46.41 | 37.11-59.54 | 51 |
| | Hard | Fatheads | 62.81 | 54.99-73.69 | 62.81 | 54.99-73.69 | 59.30 | 50.87-70.34 | 60 |
| | Soft | Bluegills | 25.05 | 19.03-33.53 | 25.05 | 19.03-33.53 | 25.05 | 19.03-33.53 | 22 |
| | Soft | Goldfish | 64.74 | 57.17-75.48 | 64.74 | 57.17-75.48 | 64.74 | 57.17-75.48 | 68 |
| | Soft | Guppies | 74.83 | 58.75-95.32 | 74.83 | 58.75-95.32 | 74.83 | 58.75-95.32 | 68 |
| Ethylbenzene (B.P. 134-136) | Soft | Fatheads | 48.51 | 38.90-62.83 | 48.51 | 38.90-62.83 | 48.51 | 38.90-62.83 | 40 |
| | Hard | Fatheads | 42.33 | 33.52-53.47 | 42.33 | 33.52-53.47 | 42.33 | 33.52-53.47 | 36 |
| | Soft | Bluegills | 35.08 | 26.74-43.67 | 32.00 | 32.00-32.00 | 32.00 | 32.00-32.00 | 29 |
| | Soft | Goldfish | 94.44 | 79.62-110.08 | 94.44 | 79.62-110.08 | 94.44 | 79.62-110.08 | 73 |
| | Soft | Guppies | 97.10 | 81.45-114.58 | 97.10 | 81.45-114.58 | 97.10 | 81.45-114.58 | 78 |

---

[a] Modified from Pickering and Henderson, 1966.

Table 55. Comparison of Acute Toxicity of Petrochemicals to Different Species of Fish[*a]

| COMPOUND | 96-Hr $TL_m$ and 95-Percent Confidence Limit for Organism (mg/1) | | | |
|---|---|---|---|---|
| | Fatheads | Bluegills | Goldfish | Guppies |
| Styrene | 46.41(37.11-59.54) | 25.05(19.03-33.53) | 64.74(57.17-75.48) | 74.83(58.75-95.32) |
| Ethylbenzene | 48.51(38.90-62.83) | 32.00(32.00-32.00) | 94.44(79.62-110.1) | 97.10(81.45-114.6) |

[*] Under standard conditions - soft water as diluent; temperature 25°C.

[a] Modified from Pickering and Henderson, 1966.

Table 56. Significance of Difference Between Estimated 96-Hr $TL_m$ Values in Soft Water for Different Species*a

| COMPOUND | Significance of Difference in 96-Hr $TL_m$ | | | | | |
|---|---|---|---|---|---|---|
| | Fathead vs. Bluegill | Fathead vs. Goldfish | Fathead vs. Guppy | Bluegill vs. Goldfish | Bluegill vs. Guppy | Goldfish vs. Guppy |
| Styrene | 0.13025 | 0.11454 | 0.04466 | 0.38559 | 0.32445 | -0.10309 |
| Ethylbenzene | 0.03298 | 0.27086 | 0.27176 | 0.37429 | 0.38083 | -0.09513 |

* The 2 $TL_m$ estimates will be judged significantly different if number is $\geq 0$.

[a] Modified from Pickering and Henderson, 1966.

## 6. Effects on Microorganisms

Limited information has recently become available concerning the effects of styrene and α-methylstyrene on algae, molds, and soil bacteria. Using growth and vitality as parameters of a toxic effect, Munjko and Grbić (1977) examined numerous species of algae and molds exposed to these chemicals in the nutritive media. Their results are summarized in Tables 57, 58, 59, and 60. It was apparent that styrene was the most toxic to algae, but neither compound, when present at levels less than 0.5%, had a marked effect on algae growth. Molds, on the other hand, were more sensitive to α-methylstyrene, although concentrations required to inhibit growth were quite high (≥1%). At a level of 10% in the growth medium, α-methylstyrene completely inhibited mold growth. It was not determined whether any of the test species of mold could utilize styrene or α-methylstyrene as a sole carbon source.

Additional studies have been conducted with strains of Streptomycetes isolated from soils and polluted river water to determine the effects of styrene and α-methylstyrene on growth and physiologic characteristics (Grbić and Munjko, 1977). Growth of streptomycetes on starvation media (agar as only carbon source) was attained in the presence of styrene and α-methylstyrene at concentrations up to five and seven percent, respectively (Tables 61 and 62). None of the strains isolated from soils, however, were able to grow in the presence of five percent test chemical. Further testing demonstrated that both styrene and α-methylstyrene disturb streptomycetes homeostasis by causing morphological alterations and an inhibition of the ability to decompose macromolecules such as cellulose and gelatin.

A second series of experiments conducted by Grbić and Munjko (1977) examined the ability of streptomycetes to utilize styrene and α-methylstyrene

Table 57. Vitality and Growth of Algae in Water with Addition of Styrene[a]

| Species of algae | Concentration of styrene in the medium (% v/v) | | | |
|---|---|---|---|---|
| | 0.01 | 0.05 | 0.1 | 0.5 |
| Chroococcus turgidus | R | R | R | S |
| Oscillatoria formosa | R | R | R | S |
| Nostoc entophytum | R | R | R | S |
| Anabaena augstumalis | R | R | R | S |
| Nitzschia palea | R | R | S | S |
| Chlamydomonas debariana var. micropapillata | R | R | R | S |
| Chlorella vulgaris var. vulgaris | R | R | R | S |
| Scenedesmus quadricauda | R | R | R | S |
| Pediastrum duplex var. rugulosum | R | R | S | O |
| Monoraphidium griffithii | R | R | R | S |
| Crucigenia triangularis | R | R | R | S |
| Hormidium flaccidum | R | R | R | S |
| Cosmarium laeve | R | R | R | S |

R = normal growth, as with the control, S = stagnancy of growth, O = inhibition of growth.

[a] Munjko and Grbić, 1977.

Table 58. Vitality and Growth of Algae in Water with Addition of Alpha-Methylstyrene[a]

| Species of algae | Concentration of alpha-methylstyrene in the medium (% v/v) | | | |
|---|---|---|---|---|
| | 0.01 | 0.05 | 0.1 | 0.5 |
| Chroococcus turgidus | R | R | R | R |
| Oscillatoria formosa | R | R | R | R |
| Nostoc entophytum | R | R | R | R |
| Anabaena augstumalis | R | R | R | S |
| Nitzschia palea | R | R | R | R |
| Chlamydomonas debariana var. micropapillata | R | R | R | R |
| Chlorella vulgaris var. vulgaris | R | R | R | R |
| Scenedesmus quadricauda | R | R | R | R |
| Pediastrum duplex var. rugulosum | R | R | R | R |
| Monoraphidium griffithii | R | R | R | R |
| Crucigenia triangularis | R | R | R | R |
| Hormidium flaccidum | R | R | R | R |
| Cosmarium laeve | R | R | R | R |

R = normal growth, as with the control, S = stagnancy of growth.

[a] Munjko and Grbić, 1977.

Table 59. Growth and Changes in Pigmentation of Molds on Sabouraud-agar with Addition of Styrene[a]

| Species of molds | Concentration of styrene in the medium (% v/v) | | | | |
|---|---|---|---|---|---|
| | 0.1 | 0.5 | 1 | 5 | 10 |
| Aspergillus niger | 4 | 4 | 4 | 3 | 1 |
| Aspergillus fumigatus | 4 | 4 | 3 | 1 | 0 |
| Aspergillus flavus | 4 | 4 | 3 | 3 | 1 |
| Collectrichum lindentia | 4 | 3 | 1 | 0 | 0 |
| Cephalosporium sp. | 4 | 4 | 3 | 1 | 0 |
| Fusarium sp. | 4 | 4 | 3 | 2 | 1 |
| Hypoxylon sp. | 4 | 3 | 2 | 0 | 0 |
| Penicillium notatum | 4 | 4 | 3 | 2 | 1 |
| Scopulariopsis sp. | 4 | 4 | 2 | 0 | 0 |
| Spicaria sp. | 4 | 4 | 2 | 0 | 0 |
| Trichoderma lignorum | 4 | 4 | 2 | 0 | 0 |
| Trichothetium roseum | 4 | 3 | 1 | 0 | 0 |
| Verticillium sp. | 4 | 4 | 2 | 1 | 0 |

4 = the growth as intensive as in the control, 3 = weaker growth and changes in pigmentation, 2 = single, weakly pigmented colonies, 1 = tiny nonpigmented colonies, 0 = inhibition of growth.

[a] Munjko and Grbić, 1977.

Table 60. Growth and Changes in Pigmentation of Molds on Sabouraud-agar with Addition of α-Methylstyrene[a]

| Species of molds | Concentration of α-methylstyrene in the medium (% v/v) | | | |
|---|---|---|---|---|
| | 0.1 | 0.5 | 1 | 5 |
| Aspergillus niger | 4 | 4 | 3 | 2 |
| Aspergillus fumigatus | 4 | 4 | 2 | 1 |
| Aspergillus flavus | 4 | 4 | 2 | 1 |
| Aspergillus candidus | 4 | 3 | 2 | 0 |
| Collectrichum lindentia | 3 | 1 | 0 | 0 |
| Cephalosporium sp. | 4 | 3 | 2 | 0 |
| Fusarium sp. | 4 | 3 | 1 | 0 |
| Hypoxylon sp. | 3 | 2 | 0 | 0 |
| Penicillium notatum | 4 | 3 | 2 | 1 |
| Scopulariopsis sp. | 4 | 2 | 1 | 0 |
| Spicaria sp. | 4 | 2 | 1 | 0 |
| Trichoderma lignorum | 4 | 3 | 1 | 0 |
| Trichothetium roseum | 4 | 3 | 1 | 0 |
| Verticillium sp. | 4 | 3 | 2 | 1 |

4 = the growth as intensive as in the control, 3 = weaker growth and changes in pigmentation, 2 = single, weakly pigmented colonies, 1 = tiny nonpigmented colonies, 0 = inhibition of growth.

[a] Munjko and Grbić, 1977.

Table 61. Growth of Streptomycetes on Mineral Agar with Addition of Styrene[a]

| Habitat | Growth | Percentage of strains on various concentrations of styrene (% v/v) | | | | |
|---|---|---|---|---|---|---|
| | | 2 | 3 | 5 | 7 | 10 |
| Soil | Ø | 15 | 40 | 100 | 100 | 100 |
| | X | 25 | 45 | 0 | 0 | 0 |
| | XX | 40 | 10 | 0 | 0 | 0 |
| | XXX | 20 | 5 | 0 | 0 | 0 |
| Water | Ø | 0 | 20 | 40 | 100 | 100 |
| | X | 60 | 60 | 60 | 0 | 0 |
| | XX | 20 | 20 | 0 | 0 | 0 |
| | XXX | 20 | 0 | 0 | 0 | 0 |
| Total | Ø | 12 | 36 | 88 | 100 | 100 |
| | X | 32 | 48 | 12 | 0 | 0 |
| | XX | 36 | 12 | 0 | 0 | 0 |
| | XXX | 20 | 4 | 0 | 0 | 0 |

---

[a] Grbić and Munjko, 1977.

Ø = growth of the strains inhibited; X = the growth weaker than on the pure mineral agar; XX = developed similarly as on the mineral agar; XXX = developed more intensive than on the mineral agar.

Table 62. Growth of Streptomycetes on Mineral Agar with Addition of α-Methylstyrene[a]

| Habitat | Growth | Percentage of strains on various concentrations α-methylstyrene (% v/v) | | | | |
|---|---|---|---|---|---|---|
| | | 2 | 3 | 5 | 7 | 10 |
| Soil | Ø | 60 | 95 | 100 | 100 | 100 |
| | X | 20 | 5 | 0 | 0 | 0 |
| | XX | 20 | 0 | 0 | 0 | 0 |
| | XXX | 0 | 0 | 0 | 0 | 0 |
| Water | Ø | 20 | 20 | 20 | 60 | 100 |
| | X | 0 | 20 | 20 | 0 | 0 |
| | XX | 40 | 20 | 20 | 0 | 0 |
| | XXX | 40 | 40 | 40 | 40 | 0 |
| Total | Ø | 52 | 80 | 84 | 92 | 100 |
| | X | 16 | 8 | 4 | 0 | 0 |
| | XX | 24 | 4 | 4 | 0 | 0 |
| | XXX | 8 | 8 | 8 | 8 | 0 |

[a] Grbić and Munjko, 1977.

Ø = growth of the strains inhibited; X = the growth weaker than on the pure mineral agar; XX = developed similarly as on the mineral agar; XXX = developed more intensive than on the mineral agar.

as sole carbon sources. None of the strains isolated from soil were able to grow in such a medium, and none of the strains were autotrophic (i.e., able to grow in a mineral solution without a carbon source). Nevertheless, four (80%) of the strains isolated from river water grew on 2% styrene, one on 3% styrene, and one on 2% α-methylstyrene. The fact that streptomycetes taken from polluted water were able to utilize styrene and to a lesser extent α-methylstyrene as a sole carbon source indicates an adaptive mechanism for habitats polluted with aromatic hydrocarbons.

In a single report abstracted from the Russian literature (Zubritskii, 1962) it is stated that ethylbenzene at concentrations at or exceeding 100 mg/ℓ adversely affected the growth of heterotrophic bacteria.

### 7. Biochemical Studies

Recent investigations at the biochemical level in mammalian systems have provided important new data regarding the potential health effects of exposure to styrene. Styrene given to rats by intraperitoneal injection for three or six consecutive days (500 mg/kg/day) caused a doubling in the activity of the xenobiotic hydroxylating enzyme p-nitroanisole O-demethylase in the liver (Parkki et al., 1976). The activity of aryl hydrocarbon hydroxylase, on the other hand, was practically unaffected. A single dose of styrene at 2 g/kg or repeated doses of 500 mg/kg nearly doubled the activity of epoxide hydrase. Thus, it appeared that the capacity of the liver to transform the epoxide metabolite of styrene to the less toxic glycol derivative may be enhanced with chronic exposures. Moreover, exposure to styrene increased the rate of glucuronide conjugation and thereby accelerated the removal of potentially toxic metabolic intermediates. In light of these results, it is not surprising that styrene oxide cannot be detected as a metabolite in vivo.

The importance of glutathione conjugation in the removal of bioactivated chemical metabolites has prompted an examination of the effect of styrene on the hepatic non-protein sulfhydryl content in mice, rats, hamsters, and guinea pigs (Vainio and Makinen, 1977). When given single intraperitoneal injections of styrene at 150 to 1000 mg/kg, a decrease in the hepatic non-protein sulfhydryl content was evident in all species. However, this depletion was most pronounced in mice (60% depletion) and much less so in rats (27% depletion). These results lead to speculation that the formation of reactive metabolites of styrene (i.e., styrene oxide) and their removal by glutathione conjugation may be species dependent. This notion is supported by the observation that mouse liver has a high epoxide-forming and a low epoxide-inactivating capability, thereby necessitating removal of epoxide intermediates by glutathione conjugation. In this context it might be hypothesized that the rat may be much less susceptible to the possible cytotoxic/carcinogenic actions of styrene than is the mouse or other rodent species.

Recent work by Lambotte-Vandepaer and coworkers (1979) has indicated that styrene administered intraperitoneally to rats will modify several liver enzyme activities. Single styrene injections (10 mg/kg - 500 mg/kg) produced altered (decreased) $K_m$ values within 12-48 hours for the enzymes benzo(a)pyrene hydroxylase, aldrin epoxidase, and styrene oxide hydrase. The $K_m$ for styrene epoxidase was unaffected. Ethylbenzene administered at 100 mg/kg had no significant effect on the $K_m$ of any of the four enzymes. Comparison of styrene effects with those produced by methylcholanthrene (2 x 40 mg/kg) administered 24 and 48 hours prior to sacrifice showed a differential effect on styrene oxide hydrase, since methylcholanthrene did not alter the $K_m$ of this enzyme. A microsome-containing fraction (S-9) prepared from the livers of rats pretreated with styrene (500 mg/kg) or methylcholanthrene (2 x 40 mg/kg) at 24 hours, or 24 and 48 hours, before sacrifice enhanced the number of mutations produced by benzo(a)pyrene (2.5-10 μg/plate) in the Ames test system. The authors postulated that this enhancement of liver activity for activating mutagens is the result of methylcholanthrene induction of benzo(a)pyrene hydroxylase, and of an inhibiting effect of styrene on epoxide hydrase which would lower the overall inactivation rate of potentially reactive species. These workers (Roberfroid, et al., 1978) have shown that this same styrene pretreatment schedule (500 mg/kg) increases the ability of liver (S-9) extract to activate acrylonitrile in the Ames assay.

The perinatal development of epoxide hydrase and glutathione transferase activities in the liver and at extrahepatic sites (liver, kidney, lungs, intestinal mucosa) has been studied by Ryan et al. (1976) using 8-$^{14}$C-styrene oxide. All extra-hepatic tissues studied showed appreciable glutathione transferase activity (rabbit, guinea pig). In the same species, kidney and intestinal mucosa showed significant epoxide hydrase activity, while very little activity could be shown in the lungs. Extra-hepatic metabolic activity in the rat did not show the significant sex difference observed for hepatic enzymes, except for lung epoxide hydrase. Perinatal development of hepatic and extrahepatic glutathione transferase activity in the rabbit proceeds at different rates; the liver activity develops more slowly. The authors postulated that this different rate of transferase development at various organ sites could affect the balance between conjugation and hydration pathways for styrene oxide. Pretreatment of rats with phenobarbital (3 x 80 mg/kg) for three days increased hepatic activities of glutathione transferase and epoxide hydrase in both sexes. Dibenzanthracene given at the same schedule did not induce either enzyme. Pregnenolone-16α-carbonitrile and tetrachloro-p-dioxin (TCDD) pretreatments of rats produced sex-related differences in effects; female rats showed better induction of both glutathione transfase and epoxide hydrase activities, although TCDD also elevated male hepatic glutathione transferase significantly. Studies of styrene biotransformation in the isolated, perfused rat liver and rabbit lung showed glutathione conjugate present in the bile and styrene glycol in the perfusate. Following administration of 0.1 m mole of labelled (8-$^{14}C$) styrene oxide in the rat liver system, 27-40% of the radioactivity was detected in the bile within 90 minutes indicating that conjugation with glutathione is a major pathway for metabolism.

A dose-related covalent binding of styrene oxide to rat liver protein and nucleic acids fractions has been reported by Marnicmi *et al*. (1977). Following intraperitoneal injection of 7-$^{3}H$ styrene oxide, covalently bound radioactivity was found in both the total liver homogenate and the microsomal fraction. Subsequent isolation of protein and nuclei acid fractions from the liver indicated that as total injected styrene oxide was increased from 50 mg/kg to 200 mg/kg, the percent of bound radioactivity increased significantly (3-17 fold). Incubation of these protein and nucleic acid fractions with styrene oxide *in vitro* along with a microsomal fraction produced covalent binding. The addition of 10 mM glutathione to the reaction mixture decreased this binding by 80-90%.

# IV. Regulations and Standards

## A. Current Regulations

### 1. Labelling Requirements

#### a. Styrene

The following label is recommended by the Manufacturing Chemists Association (MCA, 1971):

STYRENE MONOMER
WARNING! CAUSES EYE IRRITATION
VAPOR IRRITATING
COMBUSTIBLE
Avoid contact with eyes.
Avoid breathing vapors.
Avoid prolonged or repeated contact with skin.
Keep away from heat and open flame.
Use with adequate ventilation.
Keep container closed.
Wash thoroughly after handling.
FIRST AID: In case of contact, immediately flush eyes with plenty of water for at least 10 min. Call a physician.
IN CASE OF:
Fire - Use foam, dry chemical, or $CO_2$.
Spill or Leak - Flush area with water spray.

MCA Chemical Safety Data Sheet SD-37 is available. Containers of styrene monomer must also bear the red "Flammable Liquid" sticker (Sun Petroleum Products, 1975a).

#### b. α-Methylstyrene

An example of precautionary labeling for α-methylstyrene is provided below (Union Carbide, 1975):

alpha-METHYLSTYRENE
WARNING! CAUSES EYE INJURY AND SKIN IRRITATION
Avoid contact with eyes, skin, or clothing.
Avoid prolonged or repeated breathing of vapor.
Use with adequate ventilation.
In case of contact with eyes or skin, immediately flush with plenty of water for at least 15 minutes; for eyes, call a physician.
FOR INDUSTRY USE ONLY

c. Ethylbenzene

Precautionary labelling for ethylbenzene includes the red "Flammable Liquid" label and the following warning (Sun Petroleum Products, 1975b):

ETHYLBENZENE
WARNING! FLAMMABLE
VAPOR HARMFUL
DANGER! HARMFUL OR FATAL IF SWALLOWED
Keep away from heat, sparks, and open flame.
Keep container closed.
Use only with adequate ventilation.
Avoid prolonged breathing of vapor.
Avoid prolonged or repeated contact with skin.
If swallowed, do not induce vomiting, call physician immediately.
Keep out of reach of children.

Labels vary according to manufacturer, but the warning is essentially the same. Tank cars and boxcars carrying ethylbenzene must bear the ICC "Dangerous" placard (Charter Chemicals, no date).

d. Divinylbenzene

Divinylbenzene is considered a combustible liquid. Labelling requirements and warnings are essentially the same as for other compounds.

2. Food Tolerances

Federal regulations regarding the use of styrene, α-methylstyrene, ethylbenzene, and divinylbenzene are primarily concerned with their use as indirect food additives in the form of copolymers and polymers.

Regulations were found for the monomer styrene, divinylbenzene, and α-methylstyrene. The use of styrene monomer in resinous and polymeric coatings, and as an adhesive in articles intended for packaging, transporting, or holding food (21 CFR 175.300; 21 CFR 175.105) was permitted. It was limited to 5% by weight of rubber articles intended for repeated use in food storage, handling, preparing, etc. (21 CFR 177.2600). Use as a solvent for inhibitors, accelerators, and catalysts used in the production of polyester resins for articles intended for food storage, handling, and preparation was also permitted (21 CFR 177.2420). Basic polystyrene polymers for use in contact with food may not contain more than 1% by weight of total residual styrene monomer (21 CFR 177.1640). Divinylbenzene is approved for use in ion-exchange resins; adhesives; paper and paperboard in contact with aqueous, fatty, and dry foods; acrylic plastics; and semirigid and rigid PVC plastics. α-Methylstyrene is approved for similar use as well as for some rubber and sealing gasket applications (Burgess, 1978).

### 3. Standards for Human Exposure

#### a. Styrene Monomer

The U.S. Occupational Standard, time weighted average (TWA), for air has been set at 100 ppm with a ceiling concentration of 200 ppm and a peak concentration of 600 ppm/5 minutes/3 hours (EPA, 1976).

The Threshold Limit Value (TLV), established by the American Conference of Governmental and Industrial Hygienists, is also 100 ppm or approximately 420 $mg/m^3$ (ACGIH, 1974, 1977). This level produced mild, transient responses in 50% of the volunteers exposed.

The Soviet limit for exposure is 50 $mg/m^3$ or approximately 12 ppm (ACGIH, 1974).

The American National Standards Institute also recommends a TLV of 100 ppm and a ceiling value of 200 ppm (ANSI, 1968).

#### b. α-Methylstyrene

The U.S. Occupational Standard, TWA, for air and the TLV have been set at 100 ppm or approximately 480 $mg/m^3$ (EPA, 1976; ACGIH, 1974, 1977). This TLV will minimize complaints due to unpleasant odor and eye irritation.

c. Ethylbenzene

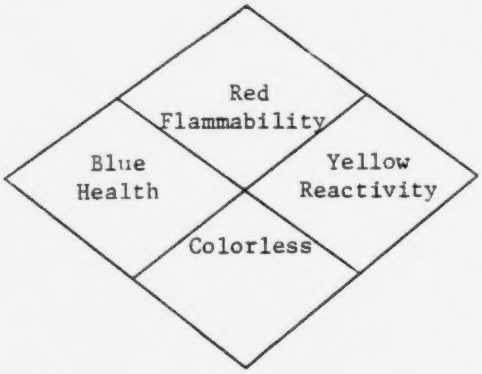
The U.S. Occupational Standard, TWA, for air and the TLV have been set at 100 ppm or approximately 435 $mg/m^3$ (EPA, 1976; ACGIH, 1974, 1977). Eye irritation will be minimal at this level.

d. Divinylbenzene

No recommended standards for human exposure are known.

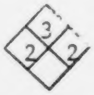
4. NFPA Hazard Identification Code

The Hazard Identification System recommended by the National Fire Protection Guide provides basic emergency information on health, flammability and reactivity. The NFPA symbol includes color and numerical codes as follows:

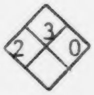


Each diamond is assigned a number from 0-4, ranging from 0 (no special hazard) to 4 (severe hazard or danger).

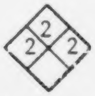
The NFPA symbols (NFPA, 1975) for the chemicals profiled in this report are:



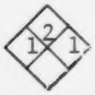
Styrene



Ethylbenzene



Divinylbenzene



α-Methylstyrene

### B. Current Handling Practices

#### 1. Special Handling in Use

##### a. Styrene

Procedures for handling styrene monomer are explained by the Manufacturing Chemists Association in Chemical Safety Data Sheet SD-37 (MCA, 1971). Normal practices associated with handling flammable organic liquids should be employed.

Avoid breathing vapors, as well as skin and eye contact. Special protective measures for use in handling styrene include: chemical safety goggles; synthetic rubber boots if foot exposure is possible; gloves; aprons; and face shields for complete face protection (MCA, 1971). Normal ventilation is usually sufficient; however, if additional ventilation equipment is installed, exhausts should be near the ground since the styrene monomer is heavier than air.

Air or oxygen supplied masks are necessary during emergencies, when the vapor concentration is greater than 2% by volume, when the oxygen level is below 16% by volume, or exposure time is greater than 30 minutes (MCA, 1971).

Styrene is not compatible with alkylation catalysts, halogens, hydrogen halides, sodium hydroxide, or glycols (which remove inhibitors), and contact with these substances should be avoided (Monsanto, 1972).

##### b. α-Methylstyrene

α-Methylstyrene is also a combustible substance and should be handled accordingly. When transferring liquids, the containers must be grounded and bonded; containers should be opened with non-sparking tools

(NIOSH-OSHA, 1975). Contact with oxidizing agents such as peroxides and halogens may cause fire and explosions. To prevent hazardous polymerization, avoid contact with peroxides, strong mineral acids, metal halides and similar catalysts (Union Carbide, 1975). As with all flammable material, avoid high temperatures and ignition sources.

Impervious clothing, rubber gloves, face shield, and splash-proof goggles are necessary to protect the body during handling. Respirators should be worn during non-routine activities and emergencies (NIOSH-OSHA, 1975). Mining enforcement and administration approval is necessary for respirators. Local exhaust ventilation is preferred in handling areas but a general mechanical system is acceptable (Union Carbide, 1975).

c. Ethylbenzene

Ethylbenzene is a NFPA No. 30 Class IC flammable liquid (Shell, 1972). Contact with acid, metallic hydrides, and iron chlorides should be avoided. Hazardous polymerization of ethylbenzene will not occur.

Contact with eyes or skin and breathing of vapors should be avoided. Special protective equipment including rubber or plastic gloves and goggles should be worn when handling ethylbenzene (Union Carbide, 1972). Respirators are not required except in enclosed space where an air supplied mask should be worn. A general mechanical ventilation system is acceptable but a local exhaust is preferable.

d. Divinylbenzene

Divinylbenzene is combustible, and exposure to flame, heat, or oxidizing materials should be avoided. Hazardous polymerization may occur at high temperatures and pressures (Dow, 1977a).

For exposure to levels up to 2% in air for one half hour or less, a full face mask and organic vapor canister should be used (Dow, 1977). Self contained breathing apparatus or equivalent is necessary during emergencies. Safety glasses and body-covering clothing provide adequate body protection.

## 2. Storage and Transport Practices

### a. Styrene

Styrene monomer is not regulated by the Department of Transportation Hazardous Materials Regulations (MCA, 1971). It is considered a Class IC flammable liquid by the U.S. Department of Labor. Open flames, local hot spots, friction, static electricity, and other ignition sources should be avoided.

Storage tanks may be constructed of steel, black iron, aluminum, and galvanized iron. Copper and copper alloys should not be used as they are subject to attack by the styrene monomer itself and the organic aldehydes and peroxides which may be present as contaminants. The tanks should be electrically bonded and grounded against static electricity; in addition, all electrical installations are subject to Article 500 of the National Electric Code concerning hazardous fire and explosion areas.

Polymerization of styrene monomer occurs readily at elevated temperatures and in the presence of both peroxides and strong acids. An inhibitor such as 4-tert-Butylcatechol (TBC) is effective in controlling polymerization. Because the inhibitor is consumed over time, periodic checks must be made. If the monomer is stored at temperatures below 70°F, once a week is sufficient. If, however, temperatures are greater than 70°F, a daily measure of inhibitor and polymerization should be made. TBC should be maintained at a level of at least 10 ppm. Dow (1967) recommends an inert gas blanket to prevent polymerization in the uninhibited vapor area (above the liquid level). Oxygen should not be entirely eliminated because TBC is ineffectual in its absence.

For further information on storage and handling practices, consult: "Storage and Handling of Styrene Type Monomers" (Dow, 1967) and "Bulk Storage of Styrene Type Monomers" (Dow, 1961).

b. α-Methylstyrene and Divinylbenzene

Storage and handling requirements of α-methylstyrene and divinylbenzene are similar to styrene (Dow, 1967). Because divinylbenzene is much less stable than styrene, TBC concentrations of 1000 ppm are necessary for storage up to 30 days at temperatures less than 90°F. Refrigerated storage and dissolved oxygen are required for effective inhibition of polymerization. α-Methylstyrene is more stable than styrene; therefore, refrigeration is not necessary.

c. Ethylbenzene

As with the other compounds, open flame, friction, static electricity, and other sources of ignition should be avoided in storage and handling.

Ethylbenzene is usually stored in carbon steel tanks (Union Carbide, 1972). Tin, aluminum, and copper tanks may cause slight discoloration with prolonged contact. Underground storage is recommended because of the relatively low flash point of 84°F. If storage is to be above ground, a flame arrestor in the vent line and inert gas blanketing are necessary.

### 3. Accident Procedures

#### a. First Aid Procedures

##### (1) Styrene

Emergency first aid procedures for exposure to styrene are from the NIOSH-OSHA Draft Technical Standards (NIOSH-OSHA, 1975) and the Manufacturing Chemists Association (MCA, 1971).

If styrene gets into the eyes, irrigate with large amounts of water for at least 15 minutes. Make sure the upper and lower eyelids are occasionally lifted to facilitate proper cleansing. Call a physician as soon as possible.

If styrene comes in contact with skin or clothing, remove all contaminated clothing and flush the skin area with water. If irritation occurs, consult a physician.

Consult a physician immediately if ingestion of styrene should occur. MCA recommends inducing the patient to vomit (except when unconscious), whereas NIOSH-OSHA states that vomiting should not be induced (MCA, 1971; NIOSH-OSHA, 1975).

If a person inhales large quantities of styrene, remove him to fresh air and get medical attention as soon as possible. Oxygen may be administered by qualified personnel.

First aid procedures for ethylbenzene, divinylbenzene, and α-methylstyrene are similar to those given for styrene.

#### b. Spill and Leak Procedures

##### (1) Styrene

Small spills may be flushed with water or absorbed with sand and removed in a container for disposal (Dow, 1977b). Large spills may be diked, pumped with water, and then recovered for disposal or purification.

Disposal of styrene wastes can be by incineration in properly designed furnaces. Water may be purified by blowing the mixture with air; the air may be burned if contamination is severe (MCA, 1971).

(2) α-Methylstyrene

Small spills can be absorbed with paper towels with subsequent evaporation and burning of the paper. Large spills should be collected with a vacuum truck and atomized in a combustion chamber (NIOSH-OSHA, 1975). Disposal should be by incineration or tertiary waste treatment (Dow, 1977c).

(3) Ethylbenzene

Flush small spill areas with water. Use of a vacuum truck and incineration of waste are recommended for large spills (Shell, 1972).

(4) Divinylbenzene

Absorb small spills in sawdust or flush with water. Dike and pump off large spills for incineration (Dow, 1977a).

TECHNICAL SUMMARY

A group of four commercially related substituted benzenes have been considered in this review: ethylbenzene, the precursor of styrene, and three vinyl substituted benzenes - styrene, α-methylstyrene, and divinylbenzene. These compounds are colorless liquids which are fairly volatile (vapor pressure ranges from 1.53 to 38.60 torr at 20°C), water insoluble (at 25°C water solubility of ethylbenzene is 161 ppm), and transparent to ultraviolet light at wavelengths greater than 300 nm. Ethylbenzene is a stable chemical while the styrene compounds are considerably more reactive, and commercial products have to be stabilized with a polymerization inhibitor.

Ethylbenzene and the styrenes are very important commercial chemicals. In 1976 the chemicals were produced in the following quantities (millions of pounds) (USITC, annual a): ethylbenzene - 7,200; styrene - 6,301; α-methylstyrene - 61.4; and divinylbenzene - not available (in 1972 production was 3.4). These compounds are produced by a diverse group of petroleum and chemical companies primarily located in Texas and Louisiana (SRI, 1977; Soder, 1977; Paul and Soder, 1977; and Chemical Prof., 1977c). Styrene oxide, a commercial chemical that has not been treated in great detail in this review, is produced in 1-2 million pounds annually (Soder, 1977). This small production volume is significant because this styrene metabolite is mutagenic and possibly carcinogenic.

Ethylbenzene is mostly produced by the liquid-phase, Friedel-Crafts alkylation of benzene with ethylene using aluminum chloride as a catalyst (Faith _et_ _al_., 1975). Small amounts of ethylbenzene are also available by fractionation of mixed xylenes. At many production facilities ethylbenzene is captively consumed in the vapor phase dehydration to styrene. α-Methylstyrene can also be made by dehydrogenation but it presently is produced as a by-product from cumene-to-phenol processes. When cumene is converted to phenol and acetone, α-methylstyrene represents about 1.7% of the total cumene conversion. Divinylbenzene is produced by dehydrogenation of isomeric diethylbenzenes to form a mixture of components, chiefly divinylbenzene and ethylvinylbenzene (Coulter et al., 1969).

There are other commercial processes where ethylbenzene or styrene are formed. Ethylbenzene is found in the mixed xylene stream obtained by catalytically reforming the naphtha stream of crude petroleum. Most of the catalytic reformate is blended into gasoline. The catalytic reformate is a source of approximately 10,000 million pounds per year of ethylbenzene, of which only a small amount of ethylbenzene is actually isolated commercially. Another non-commercial source of both ethylbenzene and styrene is pyrolysis gasoline which is obtained when paraffins, condensates, naphtha, and gas oil are cracked to produce ethylene. Pyrolysis gasoline provides about 57-96 million pounds of ethylbenzene and 228-342 million pounds of styrene annually.

Ethylbenzene is used almost totally to produce styrene while the styrenes are consumed totally in the production of plastics and rubbers. Approximately 97% to 98% of the ethylbenzene produced in the United States is consumed in styrene production; 1% to 2% is exported and less than 1% is used as solvents (Paul and Soder, 1977). The major consumption of styrene is for polystyrene (straight - 28.5%, impact - 26.5), ABS resins (7%), SAN resins (1.5%), styrene-butadiene copolymer latexes (6%), SBR elastomers (9.5%), and unsaturated polyester resins (6.5%). These products are used in consumer products (toys, tires, furniture, appliances, carpeting, etc.) and construction and industrial products (pipe, rubber products, paper coatings, ion-exchange resins, etc.). α-Methylstyrene and divinylbenzene are consumed in much smaller quantities, mostly for specialty polymers and resins. α-Methylstyrene is widely used in modified polyester and alkyd resin formulations as well as copolymers with methylmethacrylate, low molecular polymers for plasticizers in paints, waxes, etc. Its main use appears to be in ABS resins used in automobiles (Chem. Prof., 1974a). Divinylbenzene is mostly used in the production of ion-exchange resins.

The sources of environmental release of ethylbenzene and the styrenes are diverse and numerous and come from both commercial and non-commercial sources. Losses during production can result from vents on distillation columns and other process equipment, storage tank losses, miscellaneous leaks and spills, process waste waters, and solid process waters. Styrene has been detected in the vent emissions of petrochemical plants (Pervier et al., 1974) and in water effluent from latex, textile, and chemical plants (Shackelford and Keith, 1976). One estimate of production loss of ethylbenzene was 1% of production (Fuller et al., 1976) and it has been detected in several industrial chemical plant effluents.

Since the end products of ethylbenzene and the styrenes are polymers, the release of monomer should be small. However, as with all polymers, there is a small residue of monomer as well as starting material ethylbenzene which is found in the polymers. The concentration (wt %) of styrene and ethylbenzene in various grades of polystyrene can vary from 0.04 to 0.32 and 0.05 to 0.09, respectively (Crompton and Myers, 1968). Considering the production of polystyrene (3,200 million pounds in 1976) and assuming an average of 0.10 wt %

styrene and 0.06 wt % ethylbenzene, polystyrene would contain 3.2 million pounds of styrene monomer and 1.92 million pounds of ethylbenzene. Styrene and styrene oxide have been detected in air samples taken inside reinforced plastics (polyester) plants in Sweden (styrene 50-150 ppm; styrene oxide 0.03-0.2 ppm) (Pfaffli et al., 1979; Fjeldstad et al., 1979).

Environmental release from fuels, other petroleum processes, and combustion sources may equal or exceed the loss from commercial sources. Ethylbenzene has been detected in automotive exhaust (0.51 volume %) (Schofield, 1974). If it is assumed that approximately 12.5 million tons of hydrocarbons are emitted from motor vehicles (Council on Environmental Quality, 1975) and ethylbenzene is about 0.60 volume %, then roughly 280 million pounds of ethylbenzene are emitted from motor vehicle exhaust each year (about 4% of the total manufactured each year). Styrene has also been detected in hydrocarbon exhausts from spark-ignition engines (Fleming, 1970) using high m-xylene fuel compositions. In addition, styrene and methylstyrene have been identified in oxy-acetylene and oxy-ethylene flames (Crittenden and Long, 1976), which suggests that combustion sources may be a major environmental source of these compounds. Styrene has also been detected in gas products from laboratory pyrolysis of phenolic resin which are used in commercial brake linings (Fisher and Neerman, 1966), and both ethylbenzene and styrene have been identified in cigarette smoke (Johnstone et al., 1962). In addition, it is quite likely that ethylbenzene and styrene may be released from cracking plants that produce ethylene.

The environmental fate of ethylbenzene and the styrenes has not been well characterized but there is enough information to suggest some general processes. Both ethylbenzene and styrene are stable enough to be detected in ambient air and water samples. Concentrations of ethylbenzene as high as 0.01 ppm have been detected in 1961 (Altshuller and Bellar, 1963) in Los Angeles but more recent values are around 1-5 ppb (Neligan et al., 1965; Bergert et al., 1974). Styrene has also been detected at 0.2-5.0 ppb in urban air (Neligan et al., 1965; Hoskeka, 1977). Both ethylbenzene and styrene have been detected in finished drinking water (Shackelford and Keith, 1976) but little information on concentration is available.

Although both these compounds have been detected in ambient air and water, the information on their chemical stability would suggest quite different rates of degradation. Styrene is a very reactive compound which in commercial quantities has to be stabilized. Its odor threshold is low due to aerial oxidation to aldehydes and ketones. In photochemical smog chamber studies, styrene is rated as more reactive than the more reactive olefins but not as reactive as α-methylstyrene, which is ranked as one of the most reactive chemicals (Levy, 1973; Laity et al., 1973; Darnall et al., 1976). The products of photochemical oxidation have not been identified. In contrast to styrene, ethylbenzene appears to be much less reactive under simulated atmospheric conditions. Its reactivity is closer to toluene, and both have similar reaction rates with hydroxyl radical (Darnall et al., 1976). Hydroxyl radical reaction rates appear to be indicative of atmospheric reactivity. Both ethylbenzene and styrene are susceptible to metabolism by mixed cultures of microorganisms in water systems, although only indirect analytical methods ($CO_2$ evolution and BOD) were used (Ludzack and Ettinger, 1963; Price et al., 1974). A number of investigators have determined the microbial pathways of ethylbenzene and α-methylstyrene with pure cultures. Oxidation on both the ring and the side chain were noted, and which process takes place is dependent upon the substitution on the side chain. The physical properties of the compounds under study suggest that in trace quantities they are soluble in water; they will evaporate relatively rapidly and will be found in a vapor state in the atmosphere; and they are not likely to bioconcentrate in biological organisms because of their relatively high water solubility.

The human health effects of styrene, α-methylstyrene, and ethylbenzene are numerous and diverse. Most of the available health data are derived from occupational studies of workers exposed to styrene (Zielhuis, 1964; Lorimer _et al._, 1977; Lilis _et al._, 1978; Lindstrom _et al._, 1976; Meretoja _et al._, 1977; McMichael _et al._, 1976). However, concommitant exposure to other industrial chemicals commonly occurs, which prevents a definitive judgement of the effects of styrene alone. Nevertheless, it is apparent from many years of industrial observation that styrene primarily produces irritation of respiratory and conjunctival mucose at low levels of exposure (∿100 ppm) and narcosis at high levels (>800 ppm) (Stewart _et al._, 1968; Carpenter _et al._, 1944). Chronic occupational exposures to styrene are associated with neurotoxicity involving both the central nervous system and the peripheral nerves (Lilis _et al._, 1978; Lindstrom _et al._, 1976; Seppalainen and Harkonen, 1976). Workers exposed to α-methylstyrene and ethylbenzene experience symptoms qualitatively similar to those produced by styrene, although no studies have been conducted which are sufficiently validated to provide definitive dose- and time-response data.

Limited epidemiologic evidence from workers in the styrene-butadiene rubber industry has suggested an association between styrene exposure and an excess incidence of leukemia and lymphoma (McMichael _et al._, 1976; National Institute for Occupational Safety and Health, 1976). Thus far, sufficient data are not available to either confirm or deny the possible leukemogenic properties of styrene. However, a recent study (Meretoja et al., 1977) has revealed an elevated incidence of chromosome abnormalities in the cultured lymphocytes of ten chronically-exposed styrene workers. The identification of styrene metabolites in the urine strongly suggested a causal relationship between styrene absorption and chromosome damage. No information is available, however, to indicate minimum levels and duration of exposure required to produce this clastogenic response.

Controlled studies with human volunteers have established that styrene and ethylbenzene are readily absorbed across the respiratory epithelium and the skin (Astrand et al., 1974, 1975; Bardodej and Bardodejova, 1970; Dutkiewicz and Tyras, 1967, 1968). In addition, it was shown that styrene absorption via the lungs was a linear function of ventilation rate, and that light exercise could produce a dramatic rise in styrene blood levels (Astrand et al., 1975). Styrene and ethylbenzene are rapidly excreted in humans, primarily as urinary mandelic acid (Astrand et al., 1974; Bardodej and Bardodejova, 1970). Significant retention of styrene and ethylbenzene vapor may occur in the respiratory tract, and styrene can be detected in alveolar air up to 24 hours after termination of exposure.

Experiments with laboratory mammals confirmed that styrene is rapidly and extensively distributed throughout the body, regardless of the route of exposure (Danishefsky and Willhite, 1954; Sauerhoff et al., 1976; Sauerhoff and Braun, 1976). Furthermore, the excretion of styrene and its metabolites is very rapid, with elimination being essentially complete within 72 hours after exposure. However, patterns of styrene excretion appeared to be dose-dependent, suggesting that saturation of metabolic pathways may occur at high doses and lead to qualitative and quantitative differences in biotransformation and elimination mechanisms (Sauerhoff and Braun, 1976).

As a result of dose-dependent metabolism as evidenced by studies with styrene, an abnormal accumulation of certain bioactivated metabolites (presumably styrene oxide) may occur at doses which exceed detoxification capacities. At these doses, the risk of adverse physiologic reaction to a toxic metabolite is greatly increased. In rats, it is suggested that such an accumulation of activated styrene metabolites might occur at inhalation exposures exceeding 600 ppm or oral doses of 500 mg/kg (Sauerhoff and Braun, 1976). Indeed it has been shown that styrene absorption causes a dose-related depletion of liver glutathione, an essential compound for the detoxification and removal of bioactivated chemical intermediates, particularly epoxides (Vainio and Makinen, 1977). However, since styrene-mediated glutathione depletion showed considerable species variation, it is difficult to determine a specific level of exposure likely to result in abnormal risk from toxic metabolite accumulation. In addition, the possibility that chronic styrene exposure may enhance the activity of styrene detoxification mechanisms such as epoxide hydrase activity and glucuronide conjugation makes quantitative human risk evaluation uncertain (Parkki et al., 1976).

In examining the pathways of metabolism for styrene and ethylbenzene particular attention has been paid to the possibility of epoxide formation. Reactive epoxide intermediates are considered to be crucial determinants for carcinogenicity and mutagenicity of aromatic hydrocarbons. In this regard there are sufficient data to support the role of styrene oxide as an obligatory intermediate in the metabolism of styrene in animals and man (Liebman, 1975;

Liebman and Ortiz, 1969, 1970; Salmona *et al.*, 1976). With ethylbenzene, on the other hand, an epoxide intermediate does not appear to be involved in its major pathway of metabolism (Kiese and Lenk, 1973, 1974; McMahon and Sullivan, 1967, 1968; Sullivan *et al.*, 1976; Bakke and Scheline, 1970; Kaubish *et al.*, 1972).

Administration of styrene, α-methylstyrene, or ethylbenzene to animals produces a variety of toxic effects which, for the most part, resemble those seen in humans. Toxicity by acute exposure to these compounds is relatively low; oral $LD_{50}$ doses range from three to ten g/kg of body weight in rats and mice (Wolf *et al.*, 1956; Spencer *et al.*, 1942; Smyth *et al.*, 1962). Differences in species susceptibility account for wide variability in lethal doses. With acute exposure to any of these compounds, however, the symptoms are similar in all species. Both oral administration and inhalation of vapors result in irritation, incoordination, tremors, convulsions, and other signs of central nervous system involvement. Ethylbenzene appears to be somewhat less acutely toxic than styrene.

Repeated feeding or vapor inhalation of styrene, α-methylstyrene, or ethylbenzene is generally well-tolerated by most mammalian species (Spencer *et al.*, 1942; Wolf *et al.*, 1956). With rats exposed to styrene, no histopathologic lesions resulted from repeated feedings of 2000 mg/kg of body weight (5 days per week for 4 weeks) or from inhalation of vapors at a concentration of 2000 ppm (8 hours per day, 5 days per week for up to 6 months). However, with ethylbenzene, lesions of the hepatic parenchymal cells and renal tubular epithelium resulted from doses of 680 mg/kg (oral) and 1250 ppm (inhalation) using the same treatment schedule. In addition, ethylbenzene at a concentration of 600 ppm produced a degeneration of the germinal epithelium in the testes of rabbits and Rhesus monkeys. Although α-methylstyrene produced no histopathologic changes in rats or guinea pigs inhaling vapors at a concentration of 3000 ppm, significant mortality resulted during daily seven-hour exposures which continued for more than three days.

By virtue of its probable biotransformation to styrene oxide, a possible carcinogen, styrene has been considered a likely candidate for both mutagenicity and carcinogenicity testing. In microbial test systems using various strains of *Salmonella typhimurium*, styrene induced reverse mutations (base-pair substitutions) when incubated in the presence of liver microsomes to provide metabolic activation (Vainio *et al.*, 1976; DeMeester *et al.*, 1977). This mutagenic activity was presumably due to styrene oxide formed metabolically (Milvy and Garro, 1976). In eukaryotic cells (yeast and hamster) which detect forward mutations, styrene oxide was a potent direct-acting mutagen, whereas styrene yielded only equivocal results, even in the presence of liver microsomes (Loprieno *et al.*, 1976; Abbondandolo *et al.*, 1976). Poor conversion of styrene to styrene oxide and/or the extremely short half-life of styrene oxide in mammalian cells may account for the lack of an observed mutagenic effect. No information is available in the published literature concerning the mutagenicity of α-methylstyrene, ethylbenzene, or divinylbenzene.

The positive mutagenicity of styrene in certain test systems has been taken as presumptive evidence in support of possible carcinogenic activity. However, the only bioassay conducted for styrene carcinogenicity has yielded generally unreliable data (Manufacturing Chemists Association, 1978). Nevertheless, female rats inhaling styrene at concentrations of either 600 ppm or

1000 ppm (6 hours per day, 5 days per week for nearly 2 years) displayed an increase in tumors of lymphatic or hematopoietic origin. Results from other long-term studies still in progress have not yet become available. Earlier studies conducted with the presumed styrene metabolite, styrene oxide, indicated an apparent increase in malignant lymphomas among a small group of C3H mice receiving a total dose of 20 μm styrene oxide by skin painting (Kotin and Falk, 1963). Furthermore, it has been shown that exposure of cultured C3H mouse embryo cells to styrene oxide can increase the rate of neoplastic transformation induced by 3-methylcholanthrene (Nesnow and Heidelberger, 1976). This effect is thought to result either by the inhibition of epoxide hydrase, an important enzyme for detoxification, or by the depletion of glutathione. The addition of styrene to the cell culture system had no effect on transformation, however.

Thus it appears that the potential carcinogenic activity of styrene to a particular species or individual may well be determined by the steady-state level of activated metabolite (i.e., styrene oxide) produced in target organ cells. Moreover, it is not known whether different organs or heterogeneous cell populations in the same individual may have differing capacities for conversion of styrene to the epoxide and for the enzymatic detoxification of potentially carcinogenic metabolites.

Information is not presently available regarding the potential for neoplastic transformation in animals or man by direct exposure to ethylbenzene, divinylbenzene, or α-methylstyrene. However, the fact that ethylbenzene is apparently not metabolized via an epoxide intermediate suggests that its activity may differ from that of styrene.

Little is known concerning the effects of styrene, α-methylstyrene, divinylbenzene, or ethylbenzene on fish, plants, and other lower organisms in the environment. Both styrene and ethylbenzene are toxic to fish (Fathead, bluegill, goldfish, guppy), with lethal doses varying with the particular species employed (Pickering and Henderson, 1966). The 24-hour TLM values ranged from 35.08 to 97.10 mg/ℓ with ethylbenzene and from 25.05 to 74.83 mg/ℓ with styrene. Neither compound showed any evidence of cumulative toxicity over time. Styrene and α-methylstyrene are toxic to certain algae and molds, but concentrations required to produce adverse effects must exceed 0.5% (Grbić and Munjko, 1977). One author has stated that ethylbenzene inhibits the growth of heterotrophic bacteria at concentrations exceeding 100 mg/ℓ (Zubritskii, 1962).

In conclusion, it is apparent that in occupational situations styrene, α-methylstyrene, and ethylbenzene can elicit toxic responses in workers who are either acutely or chronically exposed. Among these adverse effects are an increased incidence of chromosome aberrations and a possible elevation in the rate of certain malignancies in styrene workers. There is no evidence that present levels of these chemicals in the non-occupational environment are responsible for, or may contribute to, adverse public health effects. However, since the potential carcinogenicity of styrene is presently unresolved, a definitive judgement on its health hazards must await the results of animal bioassays and more thorough epidemiologic studies. Moreover, the lack of mutagenicity, teratogenicity, and carcinogenicity data concerning ethylbenzene and α-methylstyrene, and the total lack of data concerning divinylbenzene toxicity, prevent a reliable assessment of health and environmental risks. The effect of ethylbenzene on fertility may be of particular concern in light of its damaging effects on the testicular germinal epithelium.

# References

Abbondandolo, A., Barale, R., Baroncelli, S., Bonatti, S., Bronzetti, G., Cammellini, A., Corsi, C., Corti, G., Frezza, D., Leporini, C., Loprieno, N., Mazzaccaro, A., Nieri, R., Rosellini, D., and Rossi, A.M. (1976), "Mutagenicity of Industrial Chemicals: Styrene," Assoc. Genetica Italiana, 19:113.

Abdullaeva, R.G. (1973), "Disease Rate of Synthetic Rubber Plant Personnel (According to Clinical Data for 10 Years)," Gig. Tr. Prof. Zabol., 8:140-144.

ACGIH (American Conference of Governmental Industrial Hygienists) (1974), "Documentation of Threshold Limit Values."

ACGIH (American Conference of Governmental Industrial Hygienists) (1977), "TLV's Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1977."

Aizvert, L.G. (1975), "Determination of Atrolactic Acid in Urine as an Exposure Test in Cases of α-Methylstyrene Action," Gig. Tr. Prof. Zabol., (3):38-41.

Alarie, Y. (1973), "Sensory Irritation of the Upper Airways by Airborne Chemicals," Tox. & Appl. Pharmacol., 24:279-297.

Alekperov. I.I., Knabengof, V.G., and Vinokurova, M.I. (1970a), "Oscillographic Study of Vessel Tone and Hemodynamics of Persons Working with Petroleum Hydrocarbons," Gig. Tr. Prof. Zabol., 5:22-30.

Alekperov, I.I., Vinokurova, M.L., and Knabengof, V.G. (1970b), "Combined Effect of Styrene, Butadiene, and Ethylbenzene on the Contractile Function of the Myocardium," Gig. Tr. Prof. Zabol., 5:46-55.

Aliev, T.V. and Gadzhiev, F.M. (1973), "Metabolism of Free Amino Acids in Brain Tissues During Prolonged Exposure to Low Concentrations of Styrene Vapor," Izv. Akad. Nauk Azerb. SSR, Ser. Biol. Nauk, (1): 80-85.

Altshuller, A.P. and Bellar, T.A. (1963), "Gas Chromatographic Analysis of Hydrocarbons in the Los Angeles Atmosphere," J. Air Pollution Control Assoc., 13(2):81-87.

Altshuller, A.P. and Bufalini, J.J. (1971), "Photochemical Aspects of Air Pollution: A Review," Environ. Sci. Technol., 5:39-64.

Anonymous (1976), "Styrene-leukemia Link Not Found in Study," Chem. Eng. News, 20-21.

ANSI (American National Standards Institute) (1968), Z-137.5.

Askalonov, A.A. (1973a), "Effect of Styrene on the Serotonin Content of Rat Blood and Tissues," Sb. Mater. Nauch. Konf. Fiziol., Biokhim. Farmakol. Zapad.-Sib. Ob'edin., 5th, E.F. Larin (ed.).

Askalonov, A.A. (1973b), "Effect of Styrene on the Activity of Serum Cholinesterase in Rabbits," Mater., Povolzh. Konf. Fiziol. Uchastiem Biokhim., Farmakol. Morfol., 6th, 1:332-333, G.D. Anikin (ed.).

Askalonov, A.A. (1973c), "Action of Styrene on Blood Serum Esterases," Farmakol. Toksikol, 36(5):611-613.

Askalonov, A.A. (1977), "Some Indexes of Serotonin Metabolism in Styrene Poisoning," Zdravookhr. Beloruss, (2):24-25.

Astrand, I., Kilbom, A., Övrum, P., Wahlberg, I., and Vesterberg, O. (1974), "Exposure to Styrene. I. Concentration in Alveolar Air and Blood at Rest and During Exercise and Metabolism," Work-Environ.-Hlth., 11:69-85.

Astrand, I. (1975), "Uptake of Solvents in the Blood and Tissues of Man," Scand. J. Work Environ. & Hlth., 1:199-218.

Austern, B.M., Dobbs, R.A., and Cohen, J.M. (1975), "Gas-chromatographic Determination of Selected Organic Compounds Added to Waste Water," Environ. Sci. Technol., 9(6):588-590.

Austin, G.T. (1974), "Industrially Significant Organic Chemicals - Part 8," Chem. Eng., 113-114.

Baggett, M.S., Morie, G.P., Simmons, M.W., and Lewis, J.S. (1974), "Quantitative Determination of Semivolatile Compounds in Cigarette Smoke," J. Chromatogr., 97(1):79-82.

Bakke, O.M. and Scheline, R.R. (1970), "Hydroxylation of Aromatic Hydrocarbons in the Rat," Tox. & Appl. Pharmacol., 16:691-700.

Bardodej, Z. and Bardodejova, E. (1970), "Biotransformation of Ethyl Benzene, Styrene, and Alpha-Methylstyrene in Man," Am. Ind. Hyg. Assoc. J., 206-209.

Bardodej, Z. (1978), "Styrene, its metabolism and the evaluation of hazards in industry," Scand. J. Work Environ. Health, 4(Suppl. 2):95-103.

Bashirov, A.A. (1975), "Biochemical Indexes of the Gastric Juice in the Early Diagnosis of Stomach Illnesses Under the Effect of Toxic Substances (1,3-Butadiene and Styrene)," Azerb. Med. Zh., 52(3):60-66.

Bauer, D. and Guillemin, M. (1976), "Human Exposure to Styrene. I. The Gas-chromatographic Determination of Urinary Phenylglyoxylic Acid Using Diazomethane Derivatization," Int. Arch. Occup. Environ. Hlth., 37:47-55.

Bekeshev, I.A. (1974), "State of Several Indexes of the Immunological Reactivity of Animals Under Conditions of Styrene Action at Different Temperatures," Azerb. Med. Zh., 51(3):59-62.

Belvedere, G. and Metrico L. (1967), "A Quick Method for the Determination of Benzene and Its Homologs in Reflux Waters," Med. Lav., 58(4):286-289.

Bergert, K.H., Betz, V., and Pruggmayer, D. (1974), "Untersuchung flüchtiger organischer Mikroverunreinigungen in Luft und Wasser mit Hilfe von Tiefetemperatur-Kapillar-GC/Massenspectrometric," Chromatographia, 7:115.

Bertsch, W., Anderson, E., and Holzer, G. (1975), "Trace Analysis of Organic Volatiles in Water by Gas Chromatography-Mass Spectrometry with Glass Capillary Columns," J. Chromatogr., 112:701-718.

Blake, A.J. and Rose, B.A. (1960), "The Rapid Determination of Toluene and Styrene Vapors in the Atmosphere," Analyst, 85:442-445.

Blinova, T.A. and Rylova, M.L. (1957), "Toxic Effects of Styrene and α-Methyl-styrene," Sbornik Rabot Toksikol. Lab., Gosudarst. Nauch.-Issledovatel. Inst. Gigieny Truda i Profzabolevanii, 6:6-26.

Bonatti, S., Corti, G., and Mazzaccaro, A. (1977) "Analysis of the mutations induced by styrene oxide in V79 Chinese hamster cells," Second Int. Conference on Environ. Mutagens, Edinburg, July 11-15, 1977, Abstracts, p. 151.

Boundy, R.H. and Boyer, R.F. (1952), Styrene: Its Polymers, Copolymers, and Derivatives, Am. Chem. Soc., New York.

Bravve, V.N. (1974), "Content of Vitamin $B_{12}$ in the Serum of Workers at the Krasnoyarsk Synthetic Rubber Plant," Narusheniya Metab., Tr. Nauchn. Konf. Med. Inst. Zapadn. Sib., 1st, 259-261.

Brescia, F., Mehlman, S., Pellegrini, F.C., and Stambler, S. (1974), Chemistry - A Modern Introduction, W.B. Saunders Co., p. 599-600.

Buchet, J.-P., Lauwerys, R., and Roels, H. (1974), "Evaluation de l'exposition des travailleurs au styrene par le dosage de ses metabolites urinaires: les acides mandelique et phenylglyoxylique," Arch. des Maladies Prof., de Medecine du Travail et de Securite Sociale, 35(4-5):511-516.

Budko, L.N. and Pankovets, O.A. (1968), "Dynamics of an Electroencephalogram of Rabbits after Acute Poisoning with Toluene and Styrene," Tr., Voronezh. Gos. Med. Inst., 73(4):79-82.

Burgess, K.L. (1978) Personal communication to F. Letkiewicz, July 17.

Burnham, A.K., Caldy, G.V., Fritz, J.S., Junk, G.A., Svec., H.J., and Willis, R. (1972), "Identification and Estimation of Neutral Organic Contaminants in Potable Water," Anal. Chem., 44:139.

Busk, L. (1979) "Mutagenic effects of styrene and styrene oxide," Mutation Research, 67:201-208.

Carlson, E.M. (1975), "Xylenes," Chemical Economics Handbook. Stanford Research Institute, Menlo Park, Calif.

Carpenter, C.P., Shaffer, C.B., Weil, C.S., and Smyth, H.F. (1944), "Studies on the Inhalation of 1:3-Butadiene; With a Comparison of Its Narcotic Effect With Benzol, Toluol, and Styrene, and a Note on the Elimination of Styrene by the Human," J. Ind. Hyg. Toxicol., 26(3):69-78.

Carpenter, C.P., Kinkead, E.R., Geary, D.L., Sullivan, L.J., and King, J.M. (1975), "Petroleum Hydrocarbon Toxicity Studies. V. Animal and Human Response to Vapors of Mixed Xylenes," Tox. & Appl. Pharmacol., 33:543-558.

Chakraborty, J. and Smith, J.N. (1967), "Enzymic Oxidation of Some Alkylbenzenes in Insects and Vertebrates," Biochem. J., 102:498-503.

Charter Chemicals (no date), "Ethylbenzene Technical Data Sheet," P.O. Box 5008, Houston, Texas 77012.

Chemical Engineering News (1977), "Overcapacity, Slower Demand Hit Styrene," Chem. Eng. News, April 4, 1977, 11-12.

Chemical Engineering News (1978) "Key Chemicals - Benzene," Nov. 20, 1978, p. 16.

Chemical Marketing Reporter (1977), Jan. 10, 1977, p. 26.

Chemical Marketing Reporter (1977b), 1977-1978 OPD Chemical Buyers Directory, 64th annual edition, Schnell Publ. Co., NY, NY.

Chemical Profile, Chemical Marketing Reporter (1974a), "α-Methylstyrene," December 23, 1974.

Chemical Profile, Chemical Marketing Reporter (1974b), "SB Rubber," June 24, 1974.

Chemical Profile, Chemical Marketing Reporter (1975), "Ethylbenzene," Jan. 27, 1975.

Chemical Profile, Chemical Marketing Reporter (1977a), "ABS Resins," March 28, 1977.

Chemical Profile, Chemical Marketing Reporter (1977b), "SBR," March 14, 1977.

Chemical Profile, Chemical Marketing Reporter (1977c), "α-Methylstyrene," Dec. 24, 1977.

Chemical Profile, Chemical Marketing Reporter (1977d), "Styrene," Nov. 7, 1977.

Chemical Week (1975), July 4, 1975, pp. 29-30.

Chemical Week (1976), Nov. 17, 1976, pp. 34-35.

Chemical Week (1977), 1977 Buyer's Guide Issue, Oct. 26, 1977, published by McGraw-Hill Inc., NY, NY.

Chmielewski, J., Mikulski, P., Uselis, J., and Wiglusz, R. (1973), "Rating of the Exposure to Styrene of Persons Working in the Production of Polyester Laminates," Bull. Inst. Mar. Med. Gdansk, 24(3/4):203-209.

Chmielewski, J. and Hac, E. (1976), "Clinical and Experimental Research into the Pathogenesis of Toxic Effects of Styrene," Bull. Inst. Marit. Trop. Med. Gdynia, 27(1):69-74.

Chmielewski, J. and Renke, W. (1976), "Clinical and Experimental Research into the Pathogenesis of Toxic Effects of Styrene," Bull. Inst. Marit. Trop. Med. Gdynia, 27(1):63-68.

Chukreev, E.F. (1969), "Effect of the Long-Term Action of Small Concentrations of α-Methylstyrene Alone and Mixed with 1,3-Butadiene on the Cholesterol Level in the Liver of Animals," Nauch. Tr., Omsk. Med. Inst., 88:265-268.

Cier, H.E. (1970), "Xylenes and Ethylbenzenes," Kirk-Othmer Encycl. Chem. Technol., 2nd Ed., 22:467-507.

Cirstea, M., Niculescu, V., Suhaciu, Gh., and Olaru, D.I. (1966), "Experimental Data on the Cutaneous Sensitizing Effect of Certain Compounds Used in the Manufacture of Synthetic Rubber," Stud. Cercet. Fiziol., 11(4):355-362.

Cooper, C.V., White, L.D., and Kupel, R.E. (1971), "Qualitative Limits of Detection of Specific Compounds Obtained by Trapping Gas Chromatograph Fractions with an Activated Charcoal Capillary and Analyzing with the Mass Spectrometer," Develop. Appl. Spectrosc., 9:163-170.

Coulter, K.E., Kehde, H., and Hiscock, B.F. (1969), "Styrene," Kirk-Othmer Encycl. Chem. Technol., 2nd Ed., 19:55-85.

Coulter, K.E. and Kehde, H. (1970), "Styrene Polymers. Monomers," Encycl. Polym. Sci. Technol., 13:135-155.

Council on Environmental Quality (1975), Environmental Quality, The Sixth Annual Report, available from U.S. Government Printing Office, Washington, D.C., Stock # 040-000-00337-1.

Crittenden, B.D. and Long, R. (1976), "The Mechanisms of Formation of Polynuclear Aromatic Compounds in Combustion Systems," Carcinogenesis - A Comprehensive Survey - Volume 1, Raven Press, NY, NY, pp. 209-223.

Crompton, T.R., Myers, L.W., and Blair, D. (1965), "Determination of Styrene Monomer and Other Aromatic Volatiles in Conventional and Modified Polystyrenes," Brit. Plastics, 38(12):740-746.

Crompton, T.R. and Buckley, D. (1965), "Polarographic Determination of Residual Acrylonitrile and Styrene Monomers in Styrene-Acrylonitrile Copolymers," Analyst, 90(1067):76-82.

Crompton, T.R. and Myers, L.W. (1968), "Determination of Styrene Monomer and Other Aromatic Volatiles in Conventional and Modified Polystyrenes - II," European Polymer J., 4:355-364.

Cvetanovic, R.J. (1963), "Addition of Atoms to Olefins in the Gas Phase," Advances in Photochemistry, Interscience Publishers, NY, 1:115-182.

Danishefsky, I. and Willhite, M. (1954), "The Metabolism of Styrene in the Rat," J. Biol. Chem., 211:549-553.

Darnall, K.R., Lloyd, A.C., Winer, A.M., and Pitts, J.N., Jr. (1976), "Reactivity Scale for Atmospheric Hydrocarbons Based on Reaction with Hydroxyl Radical," Environ. Sci. Technol., 10:692-696.

Davies, J.T. (1974), "Migration of Styrene Monomer from Packaging Material into Food. Experimental Verification of a Theoretical Model," J. Food Technol., 9:275-283.

Davis, J.B. and Raymond, R.L. (1961), "Oxidation of Alkyl-Substituted Cyclic Hydrocarbons by a *Nocardia* During Growth on *n*-Alkanes," Applied Microb., 9:383-388.

De Forero, I.B., De Rascovsky, E.G., De Ruiz, M. del Carmen S. (1971), "Residual Monomer in Polystyrene," Plasticos, 19(112):122-125.

De Meester, C., Poncelet, F., Roberfroid, M., Rondelet, J., and Mercier, M. (1977), "Mutagenic Activity of Styrene and Styrene Oxide. A Preliminary Study," Arch. Intl. de Physiologie et de Biochimie, 85(2):398-399.

Dilling, W.L. (1977), "Interphase Transfer Processes. II. Evaporation Rates of Chloro Methanes, Ethanes, Ethylenes, Propanes, and Propylenes from Dilute Aqueous Solutions. Comparisons with Theoretical Predictions," Environ. Sci. Technol., 11(4):405-409.

Dow Chemical (1960), "Analytical Techniques for Styrene Monomers," The Dow Chemical Co., Plastics Dept., Midland, Mich.

Dow Chemical (1961), "Bulk Storage of Styrene Type Monomers' Coatings Sales," The Dow Chemical Co., Plastics Dept., Midland, Mich.

Dow Chemical (1967), "Storage and Handling of Styrene-Type Monomers," The Dow Chemical Co., Plastics Coatings & Monomers Dept., Midland, Mich.

Dow Chemical (1977a), "Divinylbenzene 55," Material Safety Data Sheet 0076, The Dow Chemical Co., Midland, Mich.

Dow Chemical (1977b), "Styrene Monomer," Material Safety Sheet 0258, The Dow Chemical Co., Midland, Mich.

Dow Chemical (1977c), "Alpha Methylstyrene," Material Safety Data Sheet 0593, The Dow Chemical Co., Midland, Mich.

Dowty, B.J., Carlisle, D.R., and Laseter, J.L. (1975), "New Orleans Drinking Water Sources Tested by Gas Chromatography-Mass Spectrometry. Occurrence and Origin of Aromatics and Halogenated Aliphatic Hydrocarbons," Environ. Sci. Technol., 9(8):762-765.

Dutkiewicz, T. and Tyras, H. (1967), "A Study of the Skin Absorption of Ethylbenzene in Man," Brit. J. Ind. Med., 24:330-332.

Dutkiewicz, T. and Tyras, H. (1968), "Skin Absorption of Toluene, Styrene, and Xylene by Man," Brit. J. Ind. Med., 25:243.

Dwyer, F.G., Lewis, D.J., and Schneider, F.H. (1976), "Efficient, Nonpolluting Ethylbenzene Process," Chemical Engineering, Jan. 5, 1976, pp. 90-91.

El Masri, A.M., Smith, J.N., and Williams, R.T. (1958), "Studies in Detoxication. 73. The Metabolism of Alkylbenzenes: Phenylacetylene and Phenylethylene (Styrene)," Biochem. J., 68:199.

Engström, J., Astrand, I., and Wigaeus, E. (1978a), "Exposure to styrene in a polymerization plant. Uptake in the organism and concentration in subcutaneous adipose tissue," Scand. J. Work Environ. Health, 4:324-329.

Engström, J., Bjurstrom, R., Astrand, I., and Ourum, P. (1978b) "Uptake, distribution and elimination of styrene in man," Scand. J. Work Environ. Health, 4:315-323.

Engström, J. (1978), "Styrene in subcutaneous adipose tissue after experimental and industrial exposure," Scand. J. Work Environ. Health, 4(Suppl.):119-120.

Engström, K. and Rantanen, J. (1974), "A New Gas Chromatographic Method for Determination of Mandelic Acid in Urine," Intl. Arch. Arbeitsmed., 33:163-167.

Engström, K. Härkönen, H. Kalliokoski, P., and Rantanen, J. (1976), "Urinary Mandelic Acid Concentration after Occupational Exposure to Styrene and Its Use as a Biological Exposure Test," Scand. J. Work Environ. & Hlth., 2:21-26.

EPA (1976), "Preliminary Scoring of Selected Organic Air Pollutants," EPA-450/3-77-008.

Esposito, G.G. and Swann, M.H. (1965), "Determination of Styrene Monomer in Polyester Resins by Gas-Liquid Chromatography," J. Gas Chromatog., 3(6):192-193.

Esposito, G.G. (1968), "Determination of Photochemically Reactive Aromatic Hydrocarbons in Enamels and Thinners," J. Paint Technol., 40(520):214-221.

Faith, W.L., Keyes, D.B., and Clark, R.L. (1975), Industrial Chemicals, 4th Ed., John Wiley & Sons Inc., NY, pp. 365-370, 779-784.

Faustov, A.S. (1958), "Toxicity of Aromatic Hydrocarbons. I. Comparative Toxicity of Some Aromatic Hydrocarbons. II. Some Problems of the Toxic-Hygienic Properties of Aromatic Hydrocarbons," Trudy Voronezh. Med. Inst., 35:247-255, 257-262.

Faustov, A.S. (1960), "Change of Relative Toxicity in a Homologous Series of Benzene Derivatives Related to the Means of Entrance into the Organism," Tr. Voronezhsk. Med. Inst., 36:243-245.

Fernandez, J., and Caperos, J. (1977), "Studies on styrene. I. Experimental studies of the absorption and pulmonary excretion with human subjects," Int. Arch. Occup. Environ. Health, 40:1-12.

Finley, J.W. and White, J.C. (1967), "Two Methods to Determine if Styrene Monomer is Present in Milk," Bull. Environ. Contam. Toxicol., 2(1):41-46.

Fiserova-Bergerova, V., and Teisinger, J. (1965), "Pulmonary styrene vapor retention," Ind. Med. Surg., 34:620-622.

Fisher, G.E. and Neerman, J.C. (1966), "Identification of Brake Lining Constituents by Pyrolysis Gas Chromatography," Ind. Eng. Chem., Prod. Res. Develop., 5(3):288-292.

Fjeldstad, P.E., Thorud, S., and Wannag, A. (1979), "Editorial: Styrene oxide in the manufacture of reinforced polyester plastics," Scand. J. Work Environ. Health, 5:162-163.

Flieg, I., and Thiess, A. (1978) "Mutagenicity study of workers employed in the styrene and polystyrene processing and manufacturing industry," Scand. J. Work Environ. Health, 4(Suppl. 2):254-258.

Fleming, R.D. (1970), Effect of Fuel Composition on Exhaust Emissions From a Spark-Ignition Engine, U.S. Dept. of Interior, Bureau of Mines, Report of Investigations 7423.

Formaro, L. and Trasatti, S. (1968), "Capacitance Measurements on Platinum Electrodes for the Estimation of Organic Impurities in Water," Anal. Chem., 40(7):1060-1067.

Frey, H.E. (1976), "Unsaturated Polyester Resins," Chemical Economics Handbook, Stanford Research Institute, Menlo Park, Calif.

Friedman, N., Gorodetsky, M., and Mazar, Y. (1971), "Photo-oxidations of Olefins and Benzene Derivatives," J. Chem. Soc., (15):874.

Fuller, B., Hushon, J., Kornreich, M., Quellette, R., Thomas, L., and Walker, P. (1976), *Preliminary Scoring of Selected Organic Air Pollutants*, EPA Office of Air and Waste Management, EPA Contract No. 68-02-1495.

Gadzhiev, F.M. and Aliev, T.V. (1974), "New Method for Studying Free Amino Acids and Their Metabolism in Brain Tissues During the Long-Term Effect of Gasoline and Styrene Vapors," Izv. Akad. Nauk Az. SSR, Ser. Biol. Nauk, (4):112-118.

Gamberale, F. and Hultengren, M. (1974), "Exposure to Styrene. II. Psychological Functions," Work-Environ.-Hlth., 11:86-93.

Gerarde, H.W. (1963), "Toxicological Studies on Hydrocarbons," Arch. Environ. Hlth., 6:329-341.

Gibson, D.T. and Yeh, W.K. (1973), "Microbial Degradation of Aromatic Hydrocarbons," Microbial Degradation Oil Pollutants, Workshop, 33:8.

Gibson, D.T., Gschwendt, B., Yeh, W.K., and Kobal, V.M. (1973), "Initial Reactions in the Oxidation of Ethylbenzene by Pseudomonas Putida," Biochemistry, 12(8):1520-1528.

Gillette, J.R., Mitchell, J.R., and Brodie, B.B. (1974), "Biochemical Mechanisms of Drug Toxicity," Ann. Rev. Pharmacol., 14;271-287.

Glatt, H.R., Oesch, F., Frigerio, A., and Garattini, S. (1975), "Epoxides Metabolically Produced from Some Known Carcinogens and From Some Clinically Used Drugs. I. Differences in Mutagenicity," Intl. J. Cancer, 16:787-797.

Gordon, M. and Goodley, P.C. (1971), "Isolation and Characterization of Industrial Organic Pollutants in Water," Amr. Chem. Soc., Div. Water, Air Waste Chem., Gen. Pap., 11(1):91-94.

Götell, P., Axelson, O., and Lindelöf, B. (1972), "Field Studies on Human Styrene Exposure," Work-Environ.-Hlth., 9:76-83.

Grbić, D. and Munjko, I. (1977), "Growth and Changes of Streptomycetes in Media with Arylalkenes," Biológia, 32(3):179-186.

Griffin, J.D. and Glass, J.Y. (1974), "Polystyrenes," *Chemical and Process Technology Encyclopedia*, McGraw-Hill publishers, NY, pp. 914-917.

Grob, K. (1973), "Organic Substances in Potable Water and Its Precursor," J. Chromatog., 84:255.

Grob, K. and Grob, G. (1971), "Gas-Liquid Chromatographic-Mass Spectrometric Investigation of $C_6$-$C_{20}$ Organic Compounds in an Urban Atmosphere. Application of Ultratrace Analysis on Capillary Columns," J. Chromatog., 62(1):1-13.

Grob, K. and Zuercher, F. (1976), "Stripping of Trace Organic Substances from Water. Equipment and Procedure," J. Chromatog., 117(2):285-294.

Grossman, I.G. (1970), "Waterborne Styrene in a Crystalline Bedrock Aquifer in the Gales Ferry Area, Ledyard, Southeastern Connecticut," U.S. Geol. Surv., Prof. Pap., 700-B:203-209.

Guillemin, M. and Bauer, D. (1976), "Human Exposure to Styrene. II. Quantitative and Specific Gaschromatographic Analysis of Urinary Mandelic and Phenylglyoxylic Acids as an Index of Styrene Exposure," Intl. Arch. Occup. Environ. Hlth., 37:57-64.

Guillemin, M.P., and Bauer, D. (1978), "Biological monitoring of exposure to styrene by analysis of combined urinary mandelic and phenylglyoxylic acids," Am. Ind. Hyg. Assoc. J., 39(11):873-9.

Guillet, J.E., Regulski, T.W., and McAneney, T.B. (1974), "Biodegradability of Photodegraded Polymers. II. Tracer Studies of Biooxidation of Ecolyte PS Polystyrene," Environ. Sci. Technol., 8(10):923-925.

Haddad, E.A. (1976), "Polystyrene," Modern Plastics Encyclopedia 1976-1977, 53(10A):83-84.

Haken, J.K. and McKay, T.R. (1966), "Gas-Chromatographic Analysis of N,N-dialkylanilines and Vinyl Monomers in Polyester Resins," J. Gas Chromatog., 4(4):132-133.

Hannah, R.E., Cook, M.L., and Blanchette, J.A. (1967), "Gas Chromatographic Detection of Impurities in Commercial Divinylbenzene," Anal. Chem., 39(3):358-360.

Härkönen, H., Kalliokoski, P., Hietala, S., and Hernberg, S. (1974), "Concentrations of Mandelic and Phenylglyoxylic Acid in Urine as Indicators of Styrene Exposure," Work-Environ.-Hlth., 11:162-169.

Härkönen, H., Lindstrom, K., Seppalainen, A., Asp, S., and Heinberg, S. (1978), "Exposure-response relationship between styrene exposure and central nervous functions," Scand. J. Work Environ. Health, 4:53-59.

Härkönen, H. (1978), "Styrene, its experimental and clinical toxicology," Scand. J. Work Environ. Health, 4(Suppl. 2):104-113.

Hornibrook, J.M. (1962), "Manufacture of Styrene," Chem. Ind., 872-878.

Hoshika, Y. (1977), "Gas Chromatographic Determination of Styrene as Its Dibromide," J. Chromatog., 136(1):95.

Hotta, H. and Suzuki, N. (1968), "Autoxidation of Aromatic Hydrocarbons in Aqueous Solutions. XI. Termination Processes of the Autoxidations of Benzene, Toluene, and Ethylbenzene in the Aqueous Phase as Studied by Oxygen-18," Bull. Chem. Soc. Jap., 41(7):1537-1539.

Huzl, F., Sykora, J., Mainerova, J., Jankova, J., Srutek, J., Junger, V., and Lahn, V. (1967), "Health Hazards in Work With Styrene," Pracovni Lekar., 19(3):121-125.

IARC (1976), "Styrene Oxide," IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, 11:201-210.

Ikeda, M., Imamura, T., Hayashi, M., Tabushi, T., and Hara, J. (1974), "Evaluation of Hippuric, Phenylglyoxylic and Mandelic Acids in Urine as Indices of Styrene Exposure," Intl. Arch. Arbeitsmed., 32:93-101.

Ikeda, M., Ohtsuji, H., and Imamura, T. (1972), "In vivo Suppression of Benzene and Styrene Oxidation by Co-administered Toluene in Rats and Effects of Phenobarbital," Xenobiotica, 2(2):101-106.

Ivanov, S.V. (1962), "Toxicology of Ethylbenzene," Tr. Voronezhsk. Gos. Med. Inst., 47:80-82.

Ivanov, S.V. (1964), "Toxicology and Hygienic Rating of Ethylbenzene Content in the Atmosphere of Industrial Areas," Gigiena Truda i Prof. Zabolevaniya, 8(2):9-14.

Izyumova, A.S., Zlobina, N.S., and Gabrielyan, N.I. (1972), "Action of Styrene on the Reproductive Function of Rats," Vop. Gig. Tr. Profzabol., Mater. Nauch. Konf., 151-152.

Jaeger, R.J., Conolly, R.B., and Murphy, S.D. (1974), "Toxicity and Biochemical Changes in Rats After Inhalation Exposure to 1,1-Dichloroethylene, Bromobenzene, Styrene, Acrylonitrile or 2-Chlorobutadiene," Tox. Appl. Pharmacol., 29(1):81.

James, S.P. and White, D.A. (1967), "The Metabolism of Phenethyl Bromide, Styrene and Styrene Oxide in the Rabbit and Rat," Biochem. J., 104:914-921.

James, M.O., Fouts, J.R., and Bend, J.R. (1976), "Hepatic and Extrahepatic Metabolism, In Vitro, of an Epoxide (8-$^{14}$C-Styrene Oxide) in the Rabbit," Biochem. Pharmacol., 25(2):187-193.

Jensen, F. (1972), "Determination of Monomers from Polystyrene in Milk Products," Ann. 1st. Super. Sanita, 8(Pt. 2):443-448.

Jermini, C. et al. (1976), "Quantitative Determination of Various Gas-Phase Components of Side-Stream Smoke of Cigarettes in the Room Air as a Contribution to the Problem of Passive-Smoking," Intl. Arch. Occup. Environ. Hlth., 36(3):169-181.

Jersey, G., Balmer, M., Quast, J., Park, C., Schuetz, D., Beyer, J., Olson, K., McCollister, S., and Rampy, L. (1978), "Two year chronic inhalation toxicity and carcinogenicity study on monomeric styrene in rats," Dow Chemical Study for Manufacturing Chemists Association, Dec. 6, 1978.

Johnstone, R.A.W., Quan, P.M., and Carruthers, W. (1962), "Composition of Cigarette Smoke: Some Low Boiling Components," Nature, 195:1267-1269.

Kahn, J.H., LaRoe, E.G., and Conner, H.A. (1968), "Whiskey Composition: Identification of Components by Single-Pass Gas Chromatography-Mass Spectrometry," J. Food Sci., 33(4):395-400.

Kalliokoski, P. and Pfaffli, P. (1975), "Charcoal Sampling Method for Determining the Concentration of Styrene in Air," Scand. J. Work, Environ. Hlth., 1(3):193-198.

Kaubisch, N., Daly, J.W., and Jerina, D.M. (1972), "Arene Oxides as Intermediates in the Oxidative Metabolism of Aromatic Compounds. Isomerization of Methyl-Substituted Arene Oxides," Biochemistry, 11(16):3080-3088.

Kazakova, V.V. (1971a), "Effect of Styrene on Some Aspects of Natural Immunity in Laboratory Animals," Gig. Tr. Prof. Zabol., 15(2):53-54.

Kazakova, V.V. (1971b), "Effect of Styrene on the Immunobiological Reactivity of Experimental Animals," Gig. Sanit., 36(11):110-111.

Keith, L.H. (1972), "Chemical Characterization of Industrial Effluents," Amer. Chem. Soc., Div. Water, Air Waste Chem., Gen. Pap., 12(1):113-120.

Kiese, M. and Lenk, W. (1973), "ω- and (ω-1)-Hydroxylation of 4-Chloropropionanilide by Rabbits and Rabbit Liver Microsomes," Biochemical Pharmacol., 22:2565-2574.

Kiese, M. and Lenk, W. (1974), "Hydroxyacetophenones: Urinary Metabolites of Ethylbenzene and Acetophenone in the Rabbit," Xenobiotica, 4(6):337-343.

Kinlin, T.E., Muralidhara, R., Pittet, A.O., Sanderson, A., and Walradt, J.P. (1972), "Volatile Components of Roasted Filberts," J. Agr. Food Chem., 20(5):1021-1028.

Klein, O., and Zak, L. (1969), "Serum Enzyme Levels in Juveniles and Adults Engaged in the Production of Styrene-Butadiene Rubber," Prac. Lek., 21(2):56-59.

Klimina, G.M. (1974a), "Effect of Chronic Inhalation Poisoning by α-Methylstyrene on the Cholinergic Mediation System," Narusheniya Metab., Tr. Nauchn. Konf. Med. Inst. Zapadn. Sib., 1st, 291-293.

Klimina, G.M. (1974b), "Study of the Single-Dose Effect of High Concentrations of α-Methylstyrene and Acrylonitrile on the Cholinergic Mediation System," Narusheniya Metab., Tr. Nauchn. Konf. Med. Inst. Zapadn. Sib., 1st, 46-48.

Klimkova-Deutschova, E. (1962), "Neurological findings in the plastic industry with styrene workers," Int. Arch. Gewerbepath. Gewerbehyg., 19:35-50.

Konstantinovskaya, A.S. (1972), "State of the Coronary Vessel System of Workers in Butadiene-Methylstyrene Rubber Production," Vop. Gig. Tr. Profzabol., Mater. Nauch. Konf., 194-196.

Korbakova, A.I. and Fedorova, V.I. (1964), "α-Methylstyrene Toxicity," Toksikol. Novykh Prom. Khim. Veshchestv, (6):6-18.

Kotin, P. and Falk, H.L. (1963), "Organic Peroxides, Hydrogen Peroxide, Epoxides, and Neoplasia," Radiation Res. Supl., 3:193-211.

Kuz'min, V.I. (1969a), "Pathomorphological and Histochemical Changes in Respiration Organs of White Rats During the Action of α-Methylstyrene Vapors," Nauch. Tr., Omsk. Med. Inst., (88):220-225.

Kuz'min, V.I. (1969b), "Changes in the Secretion of the Epithelium of White Rat Trachea and Bronchi During the Action of α-Methylstyrene Vapors," Nauch. Tr., Omsk. Med. Inst., (88):209-214.

Laity, J.L., Burstain, J.G., and Appel, B.R. (1973), "Photochemical Smog and the Atmospheric Reactions of Solvents," in Solvents Theory and Practice, 95-112, Tess, R.W. (ed.), Advances in Chemistry Series No. 124, Am. Chem. Soc., Washington, D.C.

Lambotte-Vandepaer, M., DuVerger-van Bogaert, M., DeMeister, C., Noel, G., Poncelet, F., Roberfroid, M., and Merrier, M. (1979), "Styrene induced modifications of some rat liver enzymes involved in the activation and inactivation of xenobiotics," Biochem. Pharmacology, 28:1653-1660.

Lapkin, M. (1965), "Styrene Oxide," Kirk-Othmer Encycl. Chem. Technol., 8:289.

Larsby, B., Tham, R., Odkvist, L., Hyden, D., Bunnfors, I., and Aschan, G. (1978), "Exposure of rabbits to styrene. Electronystagmo graphic findings correlated to the styrene levels in blood and spinal fluid," Scand. J. Work Environ. Health, 4:60-65.

Leibman, K.C. (1975), "Metabolism and Toxicity of Styrene," Environ. Hlth. Perspectives, 11:115-119.

Leibman, K.C. and Ortiz, E. (1969), "Oxidation of Styrene in Liver Microsomes," Biochemical Pharmacol., 18:552-554.

Leibman, K.C. and Ortiz, E. (1970), "Epoxide Intermediates in Microsomal Oxidation of Olefins to Glycols," J. Pharmacol. Exp. Therapeutics, 173(2):242-246.

Levy, A. (1973), "The Photochemical Smog Reactivity of Organic Solvents." in Solvents Theory and Practices, Tess, R.W. (ed.), 70-94, Advances in Chemistry Series No. 124, Am. Chem. Soc., Washington, D.C.

Lhoest, G., Buchet, J.P., Lauwerys, R., and Mercier, M. (1976), "Identification by GCMS Analysis of Several Diazomethane Derivatives of Phenylglyoxylic Acid, an Urinary Metabolite of Styrene," Pharmaceutica ACTA Helvetia, 51(9):237-242.

Li, S. (1963), "Hygienic Evaluation of Styrene Air Pollution," Predel'no Dopustimye Kontsentratsii Atm. Zagryazn., (7):32-51.

Lilis, R., Lorimer, W.V., Diamond, S., and Selikoff, I.J. (1978), "Neurotoxicity of Styrene in Production and Polymerization Workers," Env. Res., 15;133-138.

Linainmaa, K., Meretoja, T., Sorsa, M., and Vainio, H. (1978), "Cytogenic effects of styrene and styrene oxide on human lymphocytes and Allium Cepa," Scand. J. Work Environ. Health, 4(Suppl. 2):142-155.

Lindström, K., Härkönen, H., and Hernberg, S. (1976), "Disturbances in Psychological Functions of Workers Occupationally Exposed to Styrene," Scand. J. Work Environ. & Hlth., 3:129-139.

Lloyd, A.C., Darnall, K.R., Winer, A.M., and Pitts, J.N., Jr. (1976), "Relative Rate Constants for Reaction of the Hydroxyl Radical with a Series of Alkanes, Alkenes, and Aromatic Hydrocarbons," J. Phys. Chem., 80:789-794.

Lonneman, W.A., Bellar, T.A., and Altshuller, A.P. (1968), "Aromatic Hydrocarbon in the Atmosphere of the Los Angeles Basin," Environ. Sci. Technol., 2(11):1017-1020.

Loprieno, N., Abbondandolo, A., Barale, R., Baroncelli, S., Bonatti, S., Bronzetti, G., Cammellini, A., Corsi, C., Corti, G., Frezza, D., Leporini, C., Mazzaccaro, A., Nieri, R., Rosellini, D., and Rossi, A.M. (1976a), "Mutagenicity of Industrial Compounds: Styrene and Its Possible Metabolite Styrene Oxide," Mutation Res., 40(4):317-324.

Loprieno, N.,Abbondandolo, A., Barale, R., Baroncelli, S., Bonatti, S., Bronzetti, G., Cammellini, A., Corsi, C., Corti, G., Frezza, D., Leporini, C., Mazzaccaro, A., Nierei, R., Rosellini, D., and Rossi, A. (1976b), "Mutagenicity of Industrial Compounds: Vinyl Chloride, Styrene and Their Possible Metabolites," Mutation Res., 38(2):114-115.

Lorimer, W.V., Lilis, R., Nicholson, W.J., Anderson, H., Fischbein, A., Daum, S., Rice, C., and Selikoff, I.J. (1977), "Clinical Studies of Styrene Workers: Preliminary Report," Proceedings of NIOSH Styrene-Butadiene Briefing, DHEW(NIOSH) Publication No. 77-129, 163-169.

Lorimer, W., Lilis, R., Fischbein, A., Daum, S., Anderson, H., Wolff, M., and Selikoff, I. (1978), "Health status of styrene-polystyrene polymerization workers," Scand. J. Work Environ. Health, 4(Suppl. 2):220-226.

Louw, C.W. and Richards, J.F. (1975), "Simple Directly Combined Gas Chromatographic-Infrared Spectrometric System for Identification of Low Molecular Weight Hydrocarbons," Appl. Spectrosc., 29(1):15-24.

Ludzack, F.J. and Ettinger, M.B. (1963), "Biodegradability of Organic Chemicals Isolated from Rivers," Purdue Univ., Eng. Bull., Ext. Ser., (115):278-282.

Lukoshkina, L.P. (1970), "Effect of Petroleum Hydrocarbons on Some Aspects of the Lipid-Protein Metabolism of Workers in Butadiene-Styrene Rubber Production," Tr. Azerb. Nauch.-Issled. Inst. Gig. Tr. Prof. Zabol., **5**:17-21.

Lukoshkina, L.P. and Alekperov, I.I. (1973), "State of Lipid-Protein Metabolism in Persons Working with 1,3-Butadiene and Styrene," Gig. Tr. Profzabol., (8):42-44.

March, J. (1968), *Advanced Organic Chemistry - Reactions, Mechanisms, and Structure*, McGraw-Hill, NY.

Marniemi, J., Suolinna, E., Kaartinen, N., and Vaimio, H. (1977), "Covalent binding of styrene oxide to rat liver macromolecules in vivo and in vitro," In: Ullrich, V., Roets, A. Estabrook, R. and Connery, A. (eds.) *Microsomes and Drug Oxidations: Proceedings of the Third International Symposium*, Pergamon Press, Oxford, 698-701.

Martin, R.L. and Winters, J.C. (1963), "Determination of Hydrocarbons in Crude Oil by Capillary-Column Gas Chromatography," Anal. Chem., **35**(12):1930-1933.

Maylin, G.A., Cooper, M.J., and Anders, M.W. (1973), "Effect of Phenobarbital Treatment on the Stereochemistry of the *in Vitro* Metabolism of Ethylbenzene," J. Med. Chem., **16**(6):606-610.

MCA (Manufacturing Chemists Association) (1971), "Properties and Essential Information for Safe Handling and Use of Styrene Monomer," Chemical Safety Data Sheet SD-37.

Manufacturing Chemists Association. (1978), Personal communication.

McDowell, D.W. (1978), "Choosing Materials for Ethylbenzene Services," Chem. Eng., Jan. 16, 1978, p. 159-160.

McKinney, R.E., Tomlinson, H.D., and Wilcox, R.L. (1956), "Metabolism of Aromatic Compounds by Activated Sludge," Sew. Ind. Wastes, **28**:547-57.

McLaughlin, J., Jr., Marliac, J-P., Verrett, M.J., Mutchler, M.K., and Fitzhugh, O.G. (1963), "The Injection of Chemicals into the Yolk Sac of Fertile Eggs Prior to Incubation as a Toxicity Test," Tox. Appl. Pharmacol., **5**:760-771.

McLaughlin, J., Jr., Marliac, J-P., Verrett, M.J., Mutchler, M.K., and Fitzhugh, O.G. (1964), "Toxicity of Fourteen Volatile Chemicals as Measured by the Chick Embryo Method," Ind. Hyg. J., 282-284.

McMahon, R.E. and Sullivan, H.R. (1966), "Microsomal Hydroxylation of Ethylbenzene. Stereospecificity and the Effect of Phenobarbital Induction," Life Sci., **7**:921-926.

McMahon, R.E. and Sullivan, H.R. (1968), "The Microsomal Hydroxylation of Ethylbenzene Stereochemical, Induction and Isotopic Studies," Microsomes and Drug Oxidation, 239-247.

McMahon, R.E., Sullivan, H.R., Craig, J.C., and Pereira, W.E., Jr. (1969), "The Microsomal Oxygenation of Ethyl Benzene: Isotopic, Stereochemical, and Induction Studies," Arch. Biochem. Biophys., 132:575-577.

McMichael, A.J., Spirtas, R., Gamble, J.F., and Tousey, P.M. (1976), "Mortality Among Rubber Workers: Relationship to Specific Jobs," J. Occup. Med., 18:178-185.

Meinhardt, T., Young, R., and Hartle, R. (1978), "Epidemiologic investigations of styrene-butadiene rubber production and reinforced plastics production," Scand. J. Work Environ. Health, 4(Suppl. 2):240-246.

Meretoja, T., Vainio, H., Sorsa, M., and Härkönen, H. (1977), "Occupational Styrene Exposure and Chromosomal Aberrations," Mutation Res., 56:193-197.

Meretoja, T. Jarventaus, H., Sorsa, M., and Vaimio, H. (1978), "Chromosome aberrations in lymphocytes of workers exposed to styrene," Scand. J. Work Environ. Health, 4(Suppl. 2):259-263.

Meretoja, T., Vainio, H., and Jarventaus, H. (1978), "Clastogenic effects of styrene exposure or bone marrow cells of rat," Toxicol. lett., 1:315-318.

Metcalf, R.L. and Lu, P-Y. (1973), "Environmental Distribution and Metabolic Fate of Key Industrial Pollutants and Pesticides in a Model Ecosystem," Univ. Ill. Water Resources Center, UILU-WRC-0069, U.S. Nat. Tech. Inform. Serv., PB225479.

Milvy, P. and Garro, A.J. (1976), "Mutagenic Activity of Styrene Oxide (1,2-Epoxyethylbenzene), A Presumed Styrene Metabolite," Mutation Res., 40:15-18.

Minaev, A.A. (1969), "Effect of Small Concentrations of $\alpha$-Methylstyrene Vapors on Man," Vop. Gig. Atmos. Vozdukha Planirovki Naselen. Mest, 42-49.

Mirzoyan, I.M. and Zhakenova, R.K. (1972), "Effect of $\alpha$-Methylstyrene and tert-Dodecyl Mercaptan on the Skin of Animals," Vop. Gig. Tr. Profzabol., Mater. Nauch. Konf., 247-249.

Mochkina, S.E. and Bravve, V.N. (1969), "Erythrocyte Volume in Rats Subjected to Chronic $\alpha$-Methylstyrene Poisoning," Tr. Krasnoyarsk. Gos. Med. Inst., 9(1):15-17.

Mochkina, S.E. and Bravve, V.N. (1969), "Vitamin $B_{12}$ Level in the Serum of Rats After Acute Administration of $\alpha$-Methylstyrene," Tr. Krasnoyarsk. Gos. Med. Inst., 9(1):13-15.

Molodyuk, A.V. (1969), "Histological and Cytochemical Study of Lymph Nodes During Chronic Poisoning with $\alpha$-Methylstyrene," Nauch. Tr., Omsk. Med. Inst., (88):226-230.

Monsanto (1972), "Styrene," Material Safety Data Sheet, Form No. 6-2489, U.S. Dept. of Labor, Workplace Standards Admin., Bureau of Labor Standards, St. Louis, Missouri.

Morneau, G.A. (1976), "ABS," Modern Plastics Encyclopedia 1976-1977, 53(10A):6-7.

Morrison, R.T. and Boyd, R.J. (1974), Organic Chemistry, Allyn & Bacon Inc., Boston, Chapters 6 & 12.

Morrow, J.E., Gritz, R.L., and Kirton, M.P. (1975), "Effects of Some Components of Crude Oil on Young Coho Salmon," Copeia, (2):326-331.

Munjko, I. and Grbić, D. (1977), "Influence of Styrene and Alpha-Methylstyrene Upon Algae and Moulds," Biologia, 32(3):173-177.

Murphy, J.E. and Forrette, J.E. (1961), "Determination of Residual Styrene and Acetophenone in Polymer Latexes," J. Appl. Polymer Sci., 5:208-211.

Murray, F.J., John, J.A., Haberstroh, H.D., Nitschke, K.D., Smith, F.A., Kociba, R.J., Olson, K.J., and Schwetz, B.A. (1976), "Teratologic Evaluation of Styrene Monomer Administered to Rats by Gavage," Toxicology Research Laboratory, Health and Environmental Research, Dow Chemical U.S.A., Midland, Mich.

Murray, F., John, J., Balmer, M., and Schuetz, B. (1978), "Teratologic evaluation of styrene given to rats and rabbits by inhalation or by gavage," Toxicology ii:335-344.

National Institute for Occupational Safety and Health (1977), Proceedings of NIOSH Styrene-Butadiene Briefing, DHEW(NIOSH) Publication No. 77-129.

Neligan, R.E. Leonard, M.J., and Bryan, R.J. (1965), "The Gas Chromatographic Determination of Aromatic Hydrocarbons in the Atmosphere," Am. Chem. Soc., Div. Water, Air Waste Chem., Preprints, 5(2):118-121.

Nesnow, S. and Heidelberger, C. (1976), "The Effect of Modifiers of Microsomal Enzymes on Chemical Oncogenesis in Cultures of C3H Mouse Cell Lines," Cancer Res., 36:1801-1808.

Nicholson, W., Selikoff, I., and Seidman, H. (1978), "Mortality experience of styrene-polystyrene polymerization workers: Initial findings," Scand. J. Work Environ. Health, 4(Suppl. 2):247-252.

NFPA (National Fire Protection Agency) (1975), "Fire Protection Guide on Hazardous Materials," 6th ed.

NIOSH-OSHA (1975), Draft Technical Standards for Alpha-Methyl Styrene, 2-Pentanone Styrene, Triphenyls, Vinyl Toluene, STEC, Part II, NTIS PB-260 432.

Nour-Eldin, F. (1968), "Phenols and Blood Coagulation," J. Biomed. Mater. Res., 2:23-42.

NSC (1971), National Safety Council Data Sheet 627, National Safety Council, Chicago, Ill.

Ogata, M. and Sugihara, R. (1978), "Quantitative determination of urinary metabolites of styrene by high-performance liquid chromatography and the variation of metabolites during lapse of time in the rat urine," Sangyo Igaku, 20(4): 218-219.

Ogleznev, G.A. (1963), "Hygienic Basis of the Maximum Allowable Concentration of α-Methylstyrene in the Water of Reservoirs," Tr. Omskogo Med. Inst., (37):309-314.

Ogleznev, G.A. (1964), "Maximum Permissible Concentration of α-Methylstyrene in Water Supplies," Gigiena i Sanit., 29(4):24-29.

Ogleznev, G.A. (1969), "Experimental Basis for the Standardization of α-Methylstyrene in Reservoir Water," Nauch. Tr., Omsk. Med. Inst., (88):19-23.

Ohtsuji, H. and Ikeda, M. (1970), "A Rapid colorimetric Method for the Determination of Phenylglyoxylic and Mandelic Acids - Its Application to the Urinalysis of Workers Exposed to Styrene Vapour," Brit. J. Ind. Med., 27:150-154.

Ohtsuji, H. and Ikeda, M. (1971), "The Metabolism of Styrene in the Rat and the Stimulatory Effect of Phenobarbital," Tox. Appl. Pharmacol., 18:321-328.

Oil and Gas Journal (1976a), Nov. 1, 1976, p. 28.

Oil and Gas Journal (1976b), Feb. 9, 1976, pp. 99-102.

Olivo, R., Ferrari, L., Manicardi, G., and Vivoli, G. (1973), "Environmental Contamination by Styrene in Certain Industries," Nuovi Ann. Ig. Microbiol., 24(3):131-138.

Oltromare, M., Desbaumes, E., Imfioff, C., and Michiels, W. (1974) Toxicologic du Styrene Monomere, Editions Medecine et Hygiene, Geneva, 100 p.

Omori, T., Yoshifumi, J., and Minoda, Y. (1974), "Microbial Oxidation of α-Methylstyrene and β-Methylstyrene," Agr. Biol. Chem., 38(2):409-415.

Opdyke, D.L.J. (1975), "Monographs on Fragrance Raw Materials - Ethylbenzene," Food Cosmet. Toxicol., 13, Suppl., 803-804.

Pagano, G., Esposito, A., Giordano, G., and Hagstrom, B. (1978), "Embryotoxic and teratogenic effects of styrene derivatives on sea urchin development," Scand. J. Work Environ. Health, 4(Suppl. 2):136-141.

Pahren, H.R., and Bloodgood, D.E. (1961), "Biological Oxidation of Several Vinyl Compounds," J. Water Pollut. Contr. Fed., 33:233-238.

Pannain, B. and Scala, A. (1960), "Electrophoretic Modifications of Serum Proteins, Lipoproteins, and Glycoproteins in Subacute Experimental Styrene Intoxication," Folia Med., 43:581-587.

Pantarotto, C., Fanelli, R., Bidoli, F., Morazzoni, P., Salmona, M., and Szczawinska, K. (1978), "Arene oxides in styrene metabolism, a new perspective in styrene toxicity?," Scand. J. Work Environ. Health, 4(Suppl. 2):67-77.

Parkes, D.G., Ganz, C.R., Polinsky, A., and Schulze, J. (1976), "A Simple Gas Chromatographic Method for the Analysis of Trace Organics in Ambient Air," Am. Ind. Hyg. Assoc. J., 37(3):165-173.

Parkki, M.G., Marniemi, J., and Vainio, H. (1976), "Action of Styrene and Its Metabolites Styrene Oxide and Styrene Glycol on Activities of Xenobiotic Biotransformation Enzymes in Rat Liver in Vivo," Tox. Appl. Pharmacol., 38:59-70.

Parkki, M.G. (1978), "The role of glutathione in the toxicity of styrene," Scand. J. Work Environ. Health, 4(Suppl. 2):53-9.

Paul, S.K. and Soder, S.L. (1977), "Ethylbenzene - Salient Statistics," Chemical Economics Handbook, Stanford Research Institute, Menlo Park, Calif.

Pavlova, L.P. and Agamova, L.P. (1974), "Effect of Low Styrene Concentrations on Lipid-Protein Metabolism in Rabbits," Gig. Tr. Prof. Zabol., (7):55-56.

Pervier, J.W., Barley, R.C., Field, D.E., Friedman, B.M., and Morris, R.B. (1974), "Survey Reports on Atmospheric Emissions from the Petrochemical Industry. Volume IV," U.S. NTIS, PB Rep. PB-245630, 287 pp.

Pfäffli, P., Vainio, H., and Hesso, A. (1979), "Styrene and styrene oxide concentrations in the air during the lamination process in the reinforced plastics industry," Scand. J. Work Environ. Health, 5:158-161.

Philippe, R., Lauwerys, R., Buchet, J.P., and Roels, H. (1971), "Évaluation de l'exposition des travailleurs au styréne par le dosage de ses métabolites urinaires: les acides mandélique et phénylglyoxylique. II. Application aux travailleurs fabriquant des polyesters," Archives des Maladies Professionnelles, de Médecine du Travail et de Sécurité Sociale, 35(6): 631-640.

Pickering, Q.H. and Henderson, C. (1966), "Acute Toxicity of Some Important Petrochemicals to Fish," J. Water Pollut. Contr. Fed., 38:1419-1429.

Pokrovskii, V.A. (1961), "Toxicology of Styrene," Gigiena Truda i Professional. Zabolevaniya, 5(5):3-7.

Pokrovskii, V.A. and Volchkova, R.I. (1968), "Effect of Some Organic Poisons on Blood Formation Processes," Tr., Voronezh. Gos. Med. Inst., 73(4):61-64.

Pratt-Johnson, J.A. (1964), "Retrobulbar Neuritis Following Exposure to Vinyl Benzene (Styrene)," Canad. Med. Assoc. J., 90:975-977.

Price, K.S., Waggy, G.T., and Conway, R.A. (1974), "Brine Shrimp Bioassay and Sea Water BOD [Biochemical Oxygen Demand] of Petrochemicals," J. Water Pollut. Contr. Fed., 46(1):63-77.

Ragelis, E.P. and Gajan, R.J. (1962), "Determination of Styrene Monomer in Polystyrene Resins by Gas Chromatography and Polarography," J. Assoc. Offic. Agr. Chemists, 45:918-921.

Ragule, N. (1974), "Embryotropic Action of Styrene," Gig. Sanit., (11):85-86.

Ramsey, J.C., and Young, J.D. (1978) "Pharmacokinetics of inhaled styrene in rats and humans," Scand. J. Work Enviorn. Health, 4(Suppl. 2):84-91.

Reichel, W.L., Prouty, R.M., and Gay, M.L. (1977), "Identification of Polychlorinated Styrene Compounds in Heron Tissues by Gas-Liquid Chromatography-Mass Spectrometry," J. Assoc. Offic. Anal. Chem., 60(1):60-62.

Riihiwaki, V., and Pfaffli, P. (1978), "Percutaneous absorption of solvent vapors in man," Scand. J. Work Environ. Health, 4:73-85.

Roberfroid, M., Poncelet, F., Lambotte-Vandepaer, M., Duverger-VanBogaert, M., DeMeester, C., and Mercier, M. (1978), "Acute biotoxic effect of styrene on rat liver. Correlation with enzyme-mediated mutagenicity of benzpyrene and acrylonitrile," Scand. J. Work Environ. Health, 4(Suppl. 2):163-8.

Rohl, A.N., Langer, A.M., Wolff, M.S., and Weisman, I. (1976), "Asbestos Exposure During Brake Lining Maintenance and Repair," Environ. Res., 12:110-128.

Rose, R.L. (1965), "[Determination of] Monomer Content of Polystyrene," Plastics, 30(338):69.

Rosen, I., Haeger-Aronsen, B., Rehnstrom, S., and Welinder, H. (1978), "Neurophysiological observations after chronic styrene exposure," Scand. J. Work Environ. Health, 4(Suppl. 2):184-194.

Roth, B., and Klimkova-Deutschova, E. (1963), "The effect of the chronic actions of industrial poisons on the electroencephalogram of man," Rev. Czech. Med., 9:217-227.

Rowe, V.K., Atchison, G.J., Luu, E.N., and Adams, E.M. (1943), "The Determination of Monomeric Styrene in Air," J. Ind. Hyg. & Tox., 25:348-353.

Roy, S.S. (1977), "Titrimetric Determination of Residual Monomers in Styrene-Acrylonitrile Copolymers," Analyst, 102(1213).

Ryan, A., James, M., Ben-Zvi, Z., Law, F., and Bend, J. (1976), "Hepatic and extra-hepatic metabolism of $C^{14}$ -styrene oxide," Environ. Health Perspect. 17:125-144.

Ryan, A.J. and Bend, J.R. (1977), "The Metabolism of Styrene Oxide in the Isolated Perfused Rat Liver," Drug Metabolism and Disposition, 5(4):363-367.

Salmona, M., Pachecka, J., Cantoni, L., Belvedere, G., Mussini, E., and Garattini, S. (1976), "Microsomal Styrene Mono-Oxygenase and Styrene Epoxide Hydrase Activities in Rats," Xenobiotica, 6(10):585-591.

Samedov, I.G., Mamedov, A.M., and Bekeshev, I.A. (1974), "Combined Effect of a Moderately High Temperature and an Intermittent Concentration of Styrene on the Reaction State of Animals," Azerb. Med. Zh., 51(10):63-68.

Sanders, W.N. and Maynard, J.B. (1968), "Capillary Gas Chromatographic Method for Determining the $C_3$-$C_{12}$ Hydrocarbons in Full-Range Motor Gasolines," Anal. Chem., 40(3):527-535.

Sauerhoff, M.W. and Braun, W.H. (1976), "The Fate of Styrene in Rats Following an Inhalation Exposure to $^{14}$C-Styrene," Toxicology Research Laboratory, Health and Environmental Research, Dow Chemical U.S.A., Midland, Mich.

Sauerhoff, M.W., Madrid, E.O., and Braun, W.H. (1976), "The Fate of Orally Administered Styrene in Rats," Toxicology Research Laboratory, Health and Environmental Research, Dow Chemical U.S.A., Midland, Mich.

Savolainen, H. (1977), "Some Aspects of the Mechanisms by which Industrial Solvents Produce Neurotoxic Effects," Chem.-Biol. Interactions, 18:1-10.

Savolainen, H., and Pfaffli, P. (1977), "Effects of chronic styrene inhalation on rat brain protein metabolism," Acta neutropath. (Berlin), 40:237-241.

Savolainen, H. and Vainio, H. (1977), "Organ Distribution and Nervous System Binding of Styrene and Styrene Oxide," Toxicology, 8:135-141.

Savolainen, H., and Pfaffli, P. (1978), "Accumulation of styrene monomer and neurochemical effects of long-term inhalation exposure in rats," Scand. J. Work Environ. Health, 4(Suppl. 2):78-83.

Schofield, K. (1974), "Problems with Flame Ionization Detectors in Automotive Exhaust Hydrocarbon Measurements," Environ. Sci. Technol., 8(9):826-834.

Schwarzmann, J.M. and Kutscha, N.P. (1971), "Accidental Styrene Poisoning," Res. in the Life Sciences, 19(3):1-3.

Seppäläinen, A.M. and Härkönen, H. (1976), "Neurophysiological Findings among Workers Occupationally Exposed to Styrene," Scand. J. Work Environ. & Hlth., 3(140-146.

Seppalainen, A.M. (1978), "Neurotoxicity of styrene in occupational and experimental exposure," Scand. J. Work Environ. Health, 4(Suppl. 2):181-3.

Sergeta, L.N., Byalko, N.K., Al'berton, N.I., and Balan, G.M. (1975), "Some Enzymological and Immunological Shifts During Prolonged Exposure to α-Methylstyrene and Butadiene in a Work Environment," Gig. Tr. Prof. Zabol., (12):51-53.

Seutter-Berlage, F., Delbressine, L.P.C., Smeets, F.L.M., and Ketelaars, H.C.J. (1978), "Identification of three sulfur-containing urinary metabolites of styrene in the rat," Xenobiotica, 8(7):413-418.

Shackelford, W.M. and Keith, L.H. (1976), "Frequency of Organic Compounds Identified in Water," EPA-600/4-76-062, U.S. Environmental Protection Agency.

Shapras, P. and Claver, G.C. (1964), "Determination of Residual Monomers and Other Volatile Components in Styrene Based Polymers by Gas Chromatography," Anal. Chem., 36(12):2282-2283.

Shell Chemical Company (1972), "Ethylbenzene," Material Safety Data Sheet MSDS-816. Shell Chem. Co., Houston, Texas.

Shugaev, B.B. and Yaroslavl, B.Sc. (1969), "Concentrations of Hydrocarbons in Tissues as a Measure of Toxicity," Arch. Environ. Hlth., 18:878-882.

Simko, A., Jindrichova, J., and Pultarova, H. (1966), "Effect of Styrene on the Health of Workers in the Production of Laminates," Pracovni Lekar., 18(8): 348-352.

Sims, P. and Grover, P.L. (1974), "Epoxides in Polycyclic Aromatic Hydrocarbon Metabolism and Carcinogenesis," Adv. Cancer Research, 20:165-274.

Sinitskii, V.G. (1969), "Indexes of Immunological Reactivity in Rabbits During the Long-Term Exposure to Small Doses of Styrene," Gig. Primen. Polim. Mater. Izdelii Nikh, (1):394-398.

Slob, A. (1973), "A New Method for Determination of Mandelic Acid Excretion of Low Level Styrene Exposure," Brit. J. Ind. Med., 30:390-393.

Smith, H.C. and Hochstettler, A. (1969), "Determination of Odor Thresholds in Air Using Carbon-14 Labeled Compounds to Monitor Concentrations," Environ. Sci. Technol., 3(2):169-170.

Smith, J.N., Smithies, R.H., and Williams, R.T. (1954), "Studies in Detoxication. 56. The Metabolism of Alkylbenzenes. Stereochemical Aspects of the Biological hydroxylation of Ethylbenzene to Methylphenylcarbinol," Biochem. J., 56:320-324.

Smyth, H.F., Jr., Carpenter, C.P., Weil, C.S., Pozzani, U.C., and Striegel, J.A. (1962), "Range-Finding Toxicity Data: List VI," Ind. Hyg. J., 95-107.

Soder, S.L. (1977), "Styrene," Chemical Economics Handbook, Stanford Research Institute, Menlo Park, Calif.

Sollenberg, J. and Baldesten, A. (1977), "Isotachophoretic Analysis of Mandelic Acid, Phenylglyoxylic Acid, Hippuric Acid and Methylhippuric Acid in Urine After Occupational Exposure to Styrene, Toluene and/or Xylene," J. Chromatog., 132:469-476.

Solov'ev, I.I. (1969), "Effect of α-Methylstyrene on Brain Tissue Respiration," Tr. Krasnoyarsk. Gos. Med. Inst., 9(1):9-11.

Solov'ev, I.I. (1974), "General and Particular Features of Cerebral Metabolic Failure Under the Effect of Different Substances on an Organism," Narusheniya Metab., Tr. Nauchn. Konf. Med. Inst. Zapadn. Sib., 1st, 255-258.

Sorsa, M. (1978), Unpublished results, Scand. J. Work Environ. Health, 4(Suppl. 2): 155.

Spencer, H.C., Irish, D.D., Adams, E.M., and Rowe, V.K. (1942), "The Response of Laboratory Animals to Monomeric Styrene," J. Ind. Hyg. & Toxicol., 24(10):295-301.

Spicer, C.W. and Jones, P.W. (1977), "The Fate of Aromatic Hydrocarbons in Photochemical Smog Systems: Toluene," J. Air Pollut. Contr. Assoc., 27: 1122-1125.

SRI (1977), 1976 Directory of Chemical Producers, Stanford Research Institute, Menlo Park, Calif.

Stavinoha, L.L. and Newman, F.M. (1972), "Isolation and Determination of Aromatics in Gasoline by Gas Chromatography," J. Chromatogr. Sci., 10(9):583-589.

Stavinoha, L.L. (1975), "Hydrocarbon-Type Analysis of Gasoline Using Stabilized Olefin Absorption and Gas Chromatography," J. Chromatogr. Sci., 72-78.

Stephens, E.R. (1973), Hydrocarbons in Polluted Air, National Technical Information Center, PB-230999, Springfield, VA.

Stewart, R.D., Dodd, H.C., Baretta, E.D., and Schaffer, A.W. (1968), "Human Exposure to Styrene Vapor," Arch. Environ. Hlth., 10:656-662.

Stobaugh, R.B. (1965), "Styrene: How, Where, Who-Future," Hydrocarbon Processing and Petroleum Refiner, 44(12):137-146.

Stoltz, D.R. and Withey, R.J. (1977), "Mutagenicity Testing of Styrene and Styrene Epoxide in Salmonella typhimurium," Bull. Environ. Contam. & Toxicol., 17(6):739-742.

Sullivan, H.R., Miller, W.M., and McMahon, R.E. (1976), "Reaction Pathways of in vivo Stereoselective Conversion of Ethylbenzene to (-)-Mandelic Acid," Xenobiotica, 6(1):49-54.

Sun Petroleum Products Company (1975a), "Styrene Monomer," Material Safety Data Sheet (0392), Sun Pet. Prod. Co., Philadelphia, Pa.

Sun Petroleum Products Company (1975b), "Ethylbenzene," Material Safety Data Sheet (0382), Sun Pet. Prod. Co., Philadelphia, Pa.

Sutton, C. and Calder, J.A. (1975), "Solubility of Alkylbenzenes in Distilled Water and Sea Water at 25.0°," J. Chem. Eng. Data, 20(3):320-322.

Teramoto, K., and Horiguchi, S. (1978), "Studies on industrial styrene poisoning. IX. Distribution of styrene in tissues of rats following repeated exposures and intraperitoneal administration of styrene," Sangyo Igaku, 20(2):122-123.

Teramoto, K., Horiguchi, S., and Kitabatake, S. (1978), "Studies on industrial styrene poisoning. VIII. Distribution and elimination of styrene in rats exposed to styrene," Sangyo Igaku, 20(2):118-119.

Teramoto, K. (1978), "Studies on styrene poisoning from the standpoint of occupational health. II. Experimental studies of the effect of styrene on humans and animals," Osaka-shiritsu Daigaku Igaku Zasshi, 27(4-6):263-277.

Thiess, A., and Friedheim, M. (1978), "Morbidity among persons employed in styrene production, polymerization, and processing plants," Scand. J. Work Environ. Health, 4(Suppl. 2):203-214.

Toxic Materials News. (1978), "EPA Seeks Data on Polyethyl Benzene Tails...," November 29, p. 358.

Union Carbide (1972), "Ethylbenzene," Material Safety Data Sheet F-43924, 4/72-5M, Union Carbide, New York, New York.

Union Carbide (1975), "Alpha-Methylstyrene," Material Safety Data Sheet F-43740A, 5/75-4M, Union Carbide, New York, New York.

U.S. Bureau of the Census (1975), U.S. Exports - Schedule B Commodity by Country, Report FT410, U.S. Gov. Printing Office, Washington, D.C.

U.S. Bureau of the Census (1976), U.S. Exports - Schedule B Commodity by Country, Report FT410, U.S. Gov. Printing Office, Washington, D.C.

U.S. International Trade Commission (Annual a), (formerly U.S. Tariff Commission), Synthetic Organic Chemicals, U.S. Production and Sales, Washington, D.C.

U.S. International Trade Commission (Annual b), (formerly U.S. Tariff Commission), Imports of Benzenoid Chemicals and Products, Washington, D.C.

Vainio, H., Pääkkönen, R., Rönnholm, K., Raunio, V., and Pelkonen, O. (1976), "A Study on the Mutagenic Activity of Styrene and Styrene Oxide," Scand. J. Work Environ. Hlth., 3:147-151.

Vainio, H., Hemminki, K., and Elovaara, E. (1977), "Toxicity of styrene and styrene oxide on chich embryos," Toxicology, 8:319-325.

Vainio, H. and Mäkinen, A. (1977), "Styrene and Acrylonitrile Induced Depression of Hepatic Nonprotein Sulfhydryl Content in Various Rodent Species," Res. Communications in Chem. Pathol. and Pharmacol., 17(1):115-124.

Van Duuren, B.L., Nelson, N., Orris, L., Palmes, E.D., and Schmitt, F.L. (1963), "Carcinogenicity of Epoxides, Lactones, and Peroxy Compounds," J. Natl. Cancer Inst., 41-55.

Veselova, V.V. and Ogleznev, G.A. (1965), "Morphological Changes in the Organs of Animals in Acute and Chronic Intoxications with α-Methylstyrene and Styrene," Nauch. Tr. Omsk. Med. Inst., (61):89-95.

Vinokurova, M.I. (1970a), "Combined Effect of Styrene, Butadiene, and Ethylbenzene on the Functional Indexes of the Cardiovascular System," Tr. Azerb. Nauch.-Issled. Inst. Gig. Tr. Prof. Zabol., 4:21-26.

Vinokurova, M.I. (1970b), "Capillaries of Workers in a Synthetic Rubber Plant," Tr. Azerb. Nauch.-Issled. Inst. Gig. Tr. Prof. Zabol., 5:56-64.

Vivoli, G. and Vecchi, G. (1974), "Study of the Urinary Excretion of Mandelic Acid as a Test of Styrene Exposure," Lavoro Umano, 26(1):1-9.

Watabe, T., Isobe, M., Sawahata, T., Yoshikawa, K., Yamada, S., and Takabatake, E. (1978), "Metabolism and mutagenicity of styrene," Scand. J. Work Environ. Health, 4(Suppl. 2):142-55.

Webb, R.G., Garrison, A.W., Keith, L.H., and McGuire, J.M. (1973), Current Practice in GC-MS Analysis of Organics in Water, NTIS #PB 224-947.

Weil, C.S., Condra, N., Haun, C., and Striegel, J.A. (1963), "Experimental Carcinogenicity and Acute Toxicity of Representative Epoxides," Am. Ind. Hyg. Assoc. J., 24:305-325.

Wells, C.B. (1963), "Stabilizing Experimentally Leached Soil Columns With Synthetic Resins," Nature, 198, 916.

Williams, H.L. (1970), "A Quarter Century of Industrial Hygiene Surveys in the Fibrous Glass Industry," Am. Ind. Hyg. Assoc. J., 31:362-367.

Wink, A. (1972), "Effect of Long-Term Exposure to Low Levels of Toxic Substances on Urinary Excretion of 17-Oxogenic Steroids and 17-Oxosteroids," Ann Occup. Hyg., 15:211-215.

Withey, J. (1978), "The toxicology of styrene monomer and its pharmacokinetics and distribution in the rat," Scand. J. Work Environ. Health, 4(Suppl. 2; 31-40.

Withey, J.R., and Collins, P.G. (1978), "Styrene Monomer in Foods: A Limited Canadian Survey," Bull. Environ. Contam. Toxicol., 19(1):86-94.

Wolf, M.A., Rowe, V.K., McCollister, D.D., Hollingsworth, R.L., and Oyen, F. (1956), "Toxicological Studies of Certain Alkylated Benzenes and Benzene," Arch. Ind. Hlth., 14:387-398.

Wolff, M. (1976), "Evidence for existence in human tissues of monomers for plastics and rubber manufacture," Environ. Health Perspectives, 17:183-187.

Wolff, M.S., Daum, S.M., Lorimer, W.V., and Selikoff, I.J. (1977), "Styrene and Related Hydrocarbons in Subcutaneous Fat from Polymerization Workers," J. Toxicol. & Environ. Hlth., 2:997-1005.

Wolff, M., Lillis, R., Lorimer, W., and Selikoff, I. (1978), "Biological indicators of exposure in styrene polymerization workers: styrene in blood and adipose tissue and mandelic and phenyl glyoxylic acids in urine," Scand. J. Work Environ. Health, 4(Suppl. 2):114-118.

Yamamoto, R.K. and Cook, W.A. (1968), "Determination of Ethylbenzene and Styrene in Air by Ultraviolet Spectrophotometry," Am. Ind. Hyg. Assoc. J., 29(3): 238-241.

Yamamoto, Y., Takamuku, S. and Sakurai, H. (1971), "γ-Radiolysis and Mercury-Photosensitized Decomposition of Ethylbenzene Vapor," Bull. Chem. Soc. Jap., 44(2):574-576.

Zakharchenko, V.I. (1969), "Morphological Changes in White Rat Brains During Chronic Poisoning With α-Methylstyrene," Nauch. Tr., Omsk. Med. Inst., (88):202-208.

Zakharchenko, V.I. (1969), "Morphohistochemical Changes in White Rat Brain During Acute Poisoning with α-Methylstyrene," Nauch. Tr., Omsk. Med. Inst., (88):196-201.

Zielhuis, R.L. (1961), "Systemic Toxicity from Exposure to Epoxy Resins, hardeners, and Styrene," J. Occup. Med., 3:25-29.

Zielhuis, R.L., Hartogensis, F., Jongh, J., Kalsbeek, J.W.H., and Van Rees, H. (1964), "The Health of Workers Processing Reinforced Polyesters," Intl. Congress for Occup. Hlth., 14th, Madrid, 1963(3):1092-1097.

Zlobina, N.S. (1963), "Toxicity of Small Concentrations of Styrene Vapors," Gigiena i Sanit., 28(5):29-35.

Zlobina, N.S., Izyumova, A.S., and Ragul'e, N.Yu. (1975). "The Effect of Low Styrene Concentrations on the Specific Functions of the Female Organism," Gig. Tr. Prof. Zabol., (12):21-25.

Zubritskii, K.V. (1962), "The Maximum Allowable Concentration of Ethylbenzene in Reservoirs," Sanit. Okhrana Vodoemov ot Zagryazneniya Prom. Stochn. Vodami, (5):62-77.